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CHEMICAL SPECIALTIES MANUFACTURERS ASSOCIATION

Product Ingredient Review Program

August 24, 1993

ORIGINAL

Dr. John Walker Executive Director ITC (TS-792) Washington, DC 20460



Dear John:

The Chemical Specialties Manufacturers Association (CSMA) on behalf of the Fabric Softener Quats Steering Committee (QSC) is responding to the ITC's February 22, 1993, letter requesting additional information on Imidazolium Quaternary Ammonium Compounds (IQAC) and Ethoxylated Quaternary Ammonium Compounds (EQAC). The QSC participants are, Croda, Inc., Stepan Company, and Witco Corporation.

Enclosed you will find five (5) copies of a July 29, 1993 compilation of additional information and responses in regard to data submissions from FSQ Steering Committee members filed in response to the 22nd Report of the TSCA Interagency Testing Committee.

Information contained in these studies should not be reviewed, abstracted, or used by persons other than EPA without the expressed written consent of the Fabric Softener Quats Joint Venture/Chemical Specialties Manufacturers Association except as required to carry out the requirements of TSCA.

If you have questions, please contact Jim T. Hill, Ph.D., Director, Product Ingredient Review Program, CSMA, at 202-872-8110.

Sincerely

Ralph Engel

President, CSMA

for the Fabric Softener Quats

Steering Committee

enclosures

cc: FSQ Steering Committee



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Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

An Expert Report Prepared for:
Fabric Softener QUATS Steering Committee

c/o CSMA PIR Program

Report Prepared by:

John A. Todhunter, Ph.D. Fellow, American Institute of Chemists Diplomate, American Board of Toxicology

Date:

July 29, 1993

Title Page

TEXT OF RESPONSES TO QUESTIONS IN INTERAGENCY TESTING COMMITTEE LETTER OF FEBRUARY 22, 1993

In Regard to the Studies Cited in a January 17, 1984 Cover Letter from Howard Hickman, Sherex Chemical Co. -

IQAC (CAS No. 68122-86-1):

1. Two acute oral toxicity studies in rats were noted in the cover letter, but only one study of this type was found by ITC and it was for CAS No. 68413-04-7, a PEQ analog.

Additional copies of the acute oral toxicity studies on CAS No. 68122-86 are provided along with this response [See Attachments 1 & 2].

2. One eye irritation study in rabbits was listed in the cover letter; two studies of this type were found but were for PEQ analogs CAS No. 68413-04-7 and CAS No. 68389-89-9.

The eye irritation studies (additional copies provided as Attachments 2 & 3) contain information specific to IQAC 68122-86-1 at pages 2 and 29 of Attachment 2 and the full text of Attachment 3. Other QUATS are noted as well in these studies.

3. One skin irritation study in rabbits was listed in the cover letter; two studies of this type were submitted, but were for PEQ analogs CAS NO. 68413-04-7 and CAS No. 68389-89-9.

The skin irritation studies (additional copies provided as Attachments 2, 4 & 5) contain information specific to IQAC 68122-86-1 at page 21 of Attachment 2 and the full text of Attachments 4 & 5. Other QUATS are noted as well in these studies.

4. One dermal sensitization study in Guinea pigs was listed in the cover letter; two studies of this type were submitted, but were for PEQ analogs CAS NO. 68413-04-7 and CAS No. 68389-89-9.

The skin sensitization studies (additional copies provided as Attachment 6) contain information specific to IQAC 68122-86-1. Other QUATS may be noted as well in these studies.

5. One biodegradation study was listed in the cover letter, but it is unclear if the submitted study is for IQAC or for an analog of IQAC.

The biodegradation study (additional copy provided, Attachment 7) contains information specific to IQAC 68122-86-1.

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PEQ (CAS No. 68410-69-5):

1. One rat acute oral toxicity study was listed in the cover letter; two studies of this type were submitted, but were for PEQ analogs CAS No. 68389-89-9 and CAS No. 68413-04-7.

The acute oral toxicity studies (additional copies provided as Attachments 8, 9, 10, 11 & 12) contain information specific to PEQ 68410-69-5. Other QUATS may be noted as well in these studies.

2. One eye irritation study in rabbits was listed in the cover letter; ftwo studies of this type were submitted, but were for PEQ analogs CAS No. 68389-89-9 and CAS No. 68413-04-7.

The eye irritation studies (additional copies provided as Attachments 8, 9, 10, 11, 13, & 14) contain information specific to PEQ 68410-69-5. Other QUATS may be noted as well in these studies.

3. One skin irritation study in rabbits was listed in the cover letter; two studies of this type were submitted, but were for PEQ analogs CAS No. 68389-89-9 and CAS No. 68413-04-7.

The skin irritation studies (additional copies provided as Attachments 8, 9, 10, 11, 15, 16 & 17) contain information specific to PEQ 68410-69-5. Other QUATS may be noted as well in these studies.

4. One skin sensitization study in rabbits was listed in the cover letter; one study of this type was submitted, but was for PEQ analog CAS No. 68389-89-9.

The skin sensitization studies (additional copies provided as Attachments 18, 19, and 20) contain information specific to PEQ 68410-69-5. Other QUATS may be noted as well in these studies.

5. One biodegradation study was listed in the cover letter, but it is unclear if the submitted study is for PEQ or an analog of PEQ.

The biodegradation study (additional copy provided, Attachment 21) contains information specific to PEQ 68410-69-5.

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In Regard to the Studies Cited in Procter & Gamble 1984a and/or Procter and Gamble 1988 Cover Letters -

IQAC (CAS No. 68122-86-1):

1. One oral absorption, distribution, and metabolism study in rats was listed in the cover letter; one study of this type was submitted for an IQAC analog (structurally different than IQAC) CAS No. 72623-82-6.

This study is considered by the submitter to be appropriate for evaluating the metabolism of CAS No. 68122-86-1 since there are no significant structural differences between 68122-86-1 (see Figure 1) and 72623-82-6 (see Figure 1) which would be expected to affect the absorption, fate, distribution, and metabolism of 72623-82-6 from oral administration in comparison to 68122-86-1. The sole difference between 68122-86-1 and 72623-82-6 is that the former is made with soft tallow and the latter is made with hydrogenated tallow as the source of the fatty amido side chains.

In both cases, intial hydrolysis in the stomach will remove fatty amido groups from the (2-fatty amido)ethyl attached to the No. 1 nitrogen of the imidazolium ring. This will generate a fatty acid residue which differs between the compounds only in the range of the carbon chain length. imidazolium function itself will remain quaternized and retain its bulky long chain alkyl moiety at the No. 2 position of the imidazolium residue's absorption ring. Clearly, this will be dictated by its charge and molecular volume: in the stomach, absorption will be poor to non-significant due to the charge. In the intestine it will be charged to a lesser degree but will be expected to complex with bile salts and be excreted in the feces. This is exactly what is observed for 72623-82-6 and there is no reasonable scientific basis to conclude that 68122-86-1 will behave any differently. Indeed, as discussed, there are ample scientific bases to conclude that 68122-86-1 will exhibit ADME behavior essentially identical to that of 72623-82-6.

2. One dermal absorption, distribution, and metabolism study in rats was listed in the cover letter; one study of this type was submitted for IQAC analog with CAS No. 72623-82-6.

This study is considered by the submitter to be appropriate for evaluating the metabolism of CAS No. 68122-86-1 since there are no significant structural differences between 68122-86-1 (see Figure 1) and 72623-82-6 (see Figure 1) which would be expected to affect the absorption, fate, distribution, and metabolism of 72623-82-6 from dermal application in comparison to 68122-86-1. The sole difference between 68122-86-1 and 72623-82-6 is that the former is made with soft tallow and the latter is made with hydrogenated tallow as the source of the fatty amido side chains.

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In both cases, dermal absorption will be poor due to the cationic charge and the molecular size. It is well established substances are poorly absorbed from the skin and, also, that increasing molecular volume decreases the rate of skin absorption for hologous compounds. There is no mechanism available on the skin for destruction of the charged nature of imidazolium group and, therefore, no mechanism to overcome this significant bar to effective dermal uptake of these substances. at the dermal pH, little hydrolysis of the substances' fatty amido side chains is expected, thus a large molecular mass To the extent that any of either substance is will be retained. absored, it will not require metabolism to be excreted (since it would already carry a charge) and - due to the fatty and charged nature of these compounds, biliary excretion can be predicted to predominate fall other modes of excretion. This is exactly what is observed for 72623-82-6 and there is no reasonable scientific conclude that 68122-86-1 will behave any differently. to as discussed, there are ample scientific bases to con-Indeed. 68122-86-1 will exhibit ADME behavior essentially clude that identical to that of 72623-82-6.

3. One mouse lymphoma study was listed in the cover letter; one study of this type was submitted for IQAC analog CAS No. 72623-82-6.

This study is considered by the submitter to be appropriate for evaluating the mutagenicity of CAS No. 68122-86-1 since there are no significant structural differences between 68122-86-1 (see Figure 1) and 72623-82-6 (see Figure 1) which would be expected to affect the mutagenic potential of 72623-82-6 in comparison to 68122-86-1. The sole difference between 68122-86-1 and 72623-82-6 is that the former is made with soft tallow and the latter is made with hydrogenated tallow as the source of the fatty amido side chains.

As can be seen from Figure 1, the only reactive center any significance in these two compounds is the fatty amido group. This could, conceivably, provide an electrophilic center for attack by a suitable nucleophile with resulting transfer of the fatty acyl group. At intracellular pH's this will require powerful nucleophile and such reactions, when they occur, (forming a known to occur preferentially to a thiol acceptor thioester). Due to the charged nature of the imidazolium group, binding to the microsomal membranes and service there as a substrate for microsomal oxidases will not be favored and, thus, the only viable mechanism for either substance to react with the is via the acyl transfer just mentioned and genetic material which for both compounds would involve essentially the same acyl transfer. Therefore, a gene toxicity test of either one of these substances will be valid as a predictor for the gene toxicity potential of the other.

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4. One <u>in vivo</u> cytogenetics study in rats was listed in the cover letter; one study of this type was submitted for IQAC ānalog CAS No. 72623-82-6.

This study is considered by the submitter to be appropriate for evaluating the clastogenic potential of CAS No. 68122-86-1 since there are no significant structural differences between 68122-86-1 (see Figure 1) and 72623-82-6 (see Figure 1) which would be expected to affect the clastogenic potential of 72623-82-6 in comparison to 68122-86-1. The sole difference between 68122-86-1 and 72623-82-6 is that the former is made with soft tallow and the latter is made with hydrogenated tallow as the source of the fatty amido side chains.

Clastogenic effects may occur by direct gene toxicity due to reaction of the clastogen with the genetic material (leading to damage of a sort requiring recombination repair or replacement of large sections of material) or by interference with chromatid separation during mitosis.

former mechanism would require a reactive center on the compound of interest (either pre-existing or formed by action of the microsomal oxidase system). As can be seen from Figure 1, the only reactive center of any significance in these two compounds the fatty amido group. This could, conceivably, provide an electrophilic center for attack by a suitable nucleophile with resulting transfer of the fatty acyl group. At intracellular pH's this will require a powerful nucleophile and such reactions, when they occur, are known to occur preferentially to a thiol acceptor (forming a thioester). Due to the charged nature of the imidazolium group, binding to the microsomal membranes and service there as a substrate for microsomal oxidases will not be favored thus, the only viable mechanism for either substance react with the genetic material is via the acyl transfer just mentioned and which for both compounds would involve essentially same acyl transfer. Therefore, a clastogenicity test of either one of these substances will be valid as a predictor the clastogenic potential of the other, if they work by a mechanism involving reaction with genetic material.

The latter mechanism would require interference with cytoskeletal functions, which could - conceivably - be produced by membrane active substances. These would, however, be physicalchemical effects involving membrane solubility which, 68122-86-1 and 72632-82-6 will be the same based on the near identicality of physical-chemical properties affecting lipid and water solubility. Therefore, a clastogenicity test of either one of these substances will be valid as a predictor for the clastogenic potential of the other, if they work by a mechanism involving interference with cytoskeletal function.

5. One teratology study in rats was listed in the cover letter; one study of this type was submitted for IQAC analog CAS No. 72623-82-6.

This study is considered by the submitter to be appropriate for evaluating the ability of CAS No. 68122-86-1 to induce developmental and teratogenic effects since there are no significant structural differences between 68122-86-1 (see Figure 1) and 72623-82-6 (see Figure 1) which would be expected to affect the developmental toxicity / teratogenic potential of 72623-82-6 in comparison to 68122-86-1. The sole difference between 68122-86-1 and 72623-82-6 is that the former is made with soft tallow and the latter is made with hydrogenated tallow as the source of the fatty amido side chains.

Neither compound (see discussion above for points Nos. 1 and 2) will be absorbed to any significant degree from the oral routes or undergo any significant metabolism. substance will have any gene toxicity potential (see discussion for point Nos. 3 and 4, above, and No. 6, below). Therefore, if substance has any developmental or teratogenic effect produced by: (a) high dose interference with maternal nutrition which, since it results from a physical-chemical effect on the gastro-intestinal tract, can not differ from one substance to the other; (b) membrane disruption or disruption of cell:cell interaction which, since this type of effect is produced by physico-chemical interaction with cell membranes, can not vary between the two compounds in question; (c) alterations of pH or electrolyte balance in the environment of the developing embryo / fetus, either of being physico-chemical effects, would be equally produced by either substance. Therefore, teratology studies on 72623-82-6 will be equally predictive for 68122-86-1.

6. One unscheduled DNA synthesis study in human diploid cells was listed in the cover letter; one study of this type was submitted for IQAC analog CAS No. 72623-82-6.

This study is considered by the submitter to be appropriate for evaluating the ability of CAS No. 68122-86-1 to induce unscheduled synthesis of DNA since there are no significant structural differences between 68122-86-1 (see Figure 1) and 72623-82-6 (see Figure 1) which would be expected to affect the general gene damaging potential of 72623-82-6 in comparison to 68122-86-1. The sole difference between 68122-86-1 and 72623-82-8 is that the former is made with soft tallow and the latter is made with hydrogenated tallow as the source of the fatty amide side chains.

Unscheduled DNA synthesis occurs as cells try to repair non-specific damage to the genetic material. This, if it is compound related, results from reaction between the genetic material and a reactive center in the compound. The center may be pre-existing in the compound or may be formed by the action of the microsomal

oxidase system. As can be seen from Figure 1, the only reactive center of any significance in these two compounds is the amido group. This could, conceivably, provide an electrophilic center for attack by a suitable nucleophile with resulting transfer of the fatty acyl group. At intracellular pH's this require a powerful nucleophile and such reactions, when they occur, are known to occur preferentially to a thiol acceptor (forming a thioester). Due to the charged nature of the imidazolium group, binding to the microsomal membranes and service there a substrate for microsomal oxidases will not be favored and, thus, the only viable mechanism for either substance to react with the genetic material is via the acyl transfer just mentioned and which for both compounds would involve essentially the acyl transfer. Therefore, an unscheduled DNA synthesis test either one of these substances will be valid as a predictor for the non-specific genetic damage potential of the either.]

7. One bioconcentration study in blugills was listed in the cover letter; one study of this type was submitted for IQAC analog CAS No. 72623-82-6.

This study is considered by the submitter to be appropriate for evaluating the ability of CAS No. 68122-86-1 to bioconcentrate since there are no significant structural differences between 68122-86-1 (see Figure 1) and 72623-82-6 (see Figure 1) which would be expected to affect the bioconcentration potential of 72623-82-6 in comparison to 68122-86-1. The sole difference between 68122-86-1 and 72623-82-6 is that the former is made with soft tallow and the latter is made with hydrogenated tallow as the source of the fatty amido side chains.

Bioconcentration is purely dictated by physico-chemical properties. So long as two substances have essentially identical physico-chemical properties and they are not metabolized in vivo to substances with distinct physico-chemical properties, a study on one will be completely predictive for the other. CAS 68122-86-1 and CAS 72623-82-6 have essentially identical octanol-water partition coefficients, essentially identical water solubilities, and will be identically metabolized (if they are metabolized at all) by loss of the fatty acyl function via hydrolysis of the fatty amido group. Therefore, there can not be any difference in the bioaccumulation potential of 68122-86-1 compared to that of 72632-82-6.

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EEQ (CAS No. 68153-35-5)

 One acute oral toxicity study in the rat was listed in the cover letter; a study of this type was submitted for PEQ analog CAS No. 68389-89-9 and PEQ CAS No. 68410-69-5.

Procter and Gamble did, indeed, submit acute oral toxicity studies on two PEQ compounds. This was done since:

- (a) Procter and Gamble has no acute oral toxicity data of its own which is specific to EEQ CAS No. 68153-35-5 since EEQ is not manufactured for fabric softener use;
- (b) Procter and Gamble wished to provide relevant information; and,
- (c) the PEQ analogs for which data was provided will accurately predict the acute oral toxicity of the EEQ.

This is because the structural differences between 68153-35-5 (see Figure 2) and 68389-89-9 (see Figure 2) or 68410-69-5 (see Figure 2) would not reasonably be expected to produce a different acute oral toxicity (in terms of potency or effects) for the PEQ compounds in comparison to EEQ. After all, EEQ is in reality a homolog of PEQ in which the average number of ethoxy units in the polyethoxy chain is less than 1.5. "Pure" EEQ would of course have only one ethoxy unit in the side chain. Thus, a distinction between commercial EEQ and PEQ is somewhat artificial in any case.

As can be seen from Figure 2 all three compounds quaternary center to which are attached two aminoalkyl groups, methyl group, and a hydroxy alkyl group (this is a polyoxyethylchain with an average number of ethoxyl units greater 1.5 the PEQs and with an avegare number of ethoxyl units of or less in EEQ). Each structure also has two tallow amide chains identically attached (to the nitrogen of the aminoalkyl These substances will all be charged, bulky species groups). like the IQAC compounds, will not absorb well from the and, gastro-intestinal tract. The acute oral toxic effects produced thus, be due to any gastrointestinal irritation which produced. Since this is a physico-chemical property, and since these compounds have similar physico-chemical properties, substances will all have similar, low, acute oral toxicity and the toxicity of one is predictive of the others.

 One acute dermal toxicity study in rabbits was listed in the cover_letter; a study of this type was submitted for PEQ analog CAS No. 68389-89-9 and PEQ CAS No. 68410-69-5.

Procter and Gamble did, indeed, submit acute dermal toxicity studies on two PEQ compounds. This was done since:

- (a) Procter and Gamble has no acute oral toxicity data of its own which is specific to EEQ CAS No. 68153-35-5 since EEQ is not manufactured for fabric softener use;
- (b) Procter and Gamble wished to provide relevant information; and,
- (c) the PEQ analogs for which data was provided will accurately predict the acute dermal toxicity of the EEQ.

This is because the structural differences between 68153-35-5 (see Figure 2) and 68389-89-9 (see Figure 2) or 68410-69-5 (see Figure 2) would not reasonably be expected to produce a different acute dermal toxicity (in terms of potency or effects) for the PEQ compounds in comparison to EEQ. After all, EEQ is in reality a homolog of PEQ in which the average number of ethoxy units in the polyethoxy chain is less than 1.5. "Pure" EEQ would of course have only one ethoxy unit in the side chain. Thus, a distinction between commercial EEQ and PEQ is somewhat artificial in any case.

As can be seen from Figure 2 all three compounds have quaternary center to which are attached two aminoalkyl groups, methyl group, and a hydroxy alkyl group (this is a polyoxyethylchain with an average number of ethoxyl units greater than ene 1.5 in the PEQs and with an avegare number of ethoxyl units of less in EEQ). Each structure also has two tallow amide 1.5 identically attached (to the nitrogen of the aminoalkyl . These substances will all be charged, bulky species groups). and, like the IQAC compounds, will not absorb well from the skin. The acute dermal toxic effects produced will, thus, be limited to effects of irritation. Since this is a physico-chemical property, and since these compounds have similar physico-chemical properties, these substances will all have similar, low, acute dermal toxicity and the toxicity of one is predictive of others.

3. One eye irritation study in rabbits was listed in the cover letter; a study of this type was submitted for PEQ analog CAS No. 68389-89-9 and PEQ CAS No. 68410-69-5.

Procter and Gamble did indeed submit eye irritation studies on two PEQ compounds. This was done since:

- (a) Procter and Gamble has no eye irritation data of its own which is specific to EEQ CAS No. 68153-35-5 since EEQ is not manufactured for fabric softener use;
- (b) Procter and Gamble wished to provide relevant information; and,
- (c) the PEQ analogs for which data was provided will accurately predict the eye irritation potential of the EEQ.

This is because the structural differences between 68153-35-5 (see Figure 2) and 68389-89-9 (see Figure 2) or 68410-69-5 (see Figure 2) would not reasonably be expected to produce a different eye irritation potential (in terms of potency or effects) for the PEQ compounds in comparison to EEQ. After all, EEQ is in reality a homolog of PEQ in which the average number of ethoxy units in the polyethoxy chain is less than 1.5. "Pure" EEQ would of course have only one ethoxy unit in the side chain. Thus, a distinction between commercial EEQ and PEQ is somewhat artificial in any case. Since these compounds produce eye irritation by a physicochemical effect, and since these compounds have similar physicochemical properties, these substances will all have similar eye irritation potential and a study of one is predictive of the others.

4. One skin irritation study in rabbits was listed in the cover letter; a study of this type was submitted for PEQ analog CAS No. 68389-89-9 and PEQ CAS No. 68410-69-5.

Procter and Gamble did indeed provide skin irritation studies on two PEQ compounds. This was done since:

- (a) Procter and Gamble has no skin irritation data of its own which is specific to EEQ CAS No. 68153-35-5 since EEQ is not manufactured for fabric softener use;
- (b) Procter and Gamble wished to provide relevant information; and,
- (c) the PEQ analogs for which data was provided will accurately predict the skin irritation potential of the EEQ.

This is because the structural differences between $68\dot{1}\dot{3}3-35.5$ (see Figure 2) and 68389-89-9 (see Figure 2) or 68410-69-5 (see

Figure 2) would not reasonably be expected to produce a different skin irritation potential (in terms of potency or effects) for the PEQ compounds in comparison to EEQ. After all, EEQ is in reality a homolog of PEQ in which the average number of ethoxy units in the polyethoxy chain is less than 1.5. "Pure" EEQ would of course have only one ethoxy unit in the side chain. Thus, a distinction between commercial EEQ and PEQ is somewhat artificial in any case. Since these compounds produce eye irritation by a physicochemical effect, and since these compounds have similar physicochemical properties, these substances will all have similar eye irritation potential and a study of one is predictive of the others.

5. One subchronic toxicity study (route not specified) was listed in the cover letter; a dermal toxicity study was submitted for PEQ analog CAS No. 68389-89-9 and PEQ CAS No. 68410-69-5.

Procter and Gamble did, indeed, submit subchronic dermal toxicity studies on two PEQ compounds. This was done since:

- (a) Procter and Gamble has no subchronic oral toxicity data of its own which is specific to EEQ CAS No. 68153-35-5 since EEQ is not manufactured for fabric softener use;
- (b) Procter and Gamble wished to provide relevant information; and,
- (c) the PEQ analogs for which data was provided will accurately predict the subchronic dermal toxicity of the EEQ.

This is because the structural differences between 68153-35-5 (see Figure 2) and 68389-89-9 (see Figure 2) or 68410-69-5 (see Figure 2) would not reasonably be expected to produce a different acute dermal toxicity (in terms of potency or effects) for the PEQ compounds in comparison to EEQ. After all, EEQ is in reality a homolog of PEQ in which the average number of ethoxy units in the polyethoxy chain is less than 1.5. "Pure" EEQ would of course have only one ethoxy unit in the side chain. Thus, a distinction between commercial EEQ and PEQ is somewhat artificial in any case.

As can be seen from Figure 2 all three compounds have a quaternary center to which are attached two aminoalkyl groups, a methyl group, and a hydroxy alkyl group (this is a polyoxyethylene chain with an average number of ethoxyl units greater than 1.5 in the PEQs and with an avegare number of ethoxyl units of 1.5 or less in EEQ). Each structure also has two tallow amide chains identically attached (to the nitrogen of the aminoalkyl groups). These substances will all be charged, bulky species and, like the IQAC compounds, will not absorb well from the skir or the gastrointestional tract. Accordingly, the dermal sub-

chronic toxic effects produced will be limited to local irritation (chemical dermatitis) and the subchronic oral effects wil be limited to effects on the gastrointestinal mucosa. Since both sorts of effects are driven by the physico-chemical properties of a substance, and since these compounds have similar physico-chemical properties, these substances will all have similar, low, subchronic (dermal or oral) toxicity potential and a study of one will be predictive of the others.

6. One Ames Salmonella/microsome plate test was listed in the cover letter; a study of this type was submitted for PEQ analog CAS No. 68389-89-9.

This study is considered by the submitter to be appropriate for evaluating the mutagenic potential of CAS No. 68153-35-5 since the structural differences between 68153-35-5 (see Figure 2) and 68389-89-9 (see Figure 2) would not be expected give 68389-89-9 any different mutagenic potential than 68153-35-5, making an Ames test of the PEQ analog an excellent index of mutagenic potential of PEQs in general and of the homologous EEQ as well. After all, EEQ is in reality a homolog of PEQ in which the average number of ethoxy units in the polyethoxy chain is less than 1.5. "Pure" EEQ would of course have only one ethoxy unit in the side chain. Thus, a distinction between commercial EEQ and PEQ is somewhat artificial in any case.

As can be seen from Figure 2, the only reactive center significance in these two compounds is the fatty amido group and this is essentially identical in both compounds. This could, conceivably, provide an electrophilic center for attack by a suitable nucleophile with resulting transfer of the fatty acyl group. At intracellular pH's this will require a powerful nucleophile and such reactions, when they occur, are known to occur preferentially to a thiol acceptor (forming a thioester). the charged nature of the ammonium group, binding to the micromembranes and service there as a substrate for microsomal oxidases will not be favored and, thus, the only viable mechanism either substance to react with the genetic material is the acyl transfer just mentioned, which for both compounds would involve essentially the same acyl transfer. Therefore, a gene toxicity test of either one of these substances will be valid as a predictor for the gene toxicity potential of the other.

7. One mouse lymphoma study was listed in the cover letter; a study of this type was submitted for PEQ analog CAS No. 68389-89-9.

This study is considered by the submitter to be appropriate for evaluating the mutagenic potential of CAS No. 68153-35-5 since the structural differences between 68153-35-5 (see Figure 2) and 68389-89-9 (see Figure 2) would not be expected give 68389-89-9 any different mutagenic potential than 68153-35-5, making a mouse lymphoma test of the PEQ analog an excellent index

of mutagenic potential of PEQs in general and of the homologous EEQ as well. After all, EEQ is in reality a homolog of PEQ in which the average number of ethoxy units in the polyethoxy chain is less than 1.5. "Pure" EEQ would of course have only one ethoxy unit in the side chain. Thus, a distinction between commercial EEQ and PEQ is somewhat artificial in any case.

can be seen from Figure 2, the only reactive center of significance in these two compounds is the fatty amido group and this is essentially identical in both compounds. This could, provide an electrophilic center for attack conceivably, suitable nucleophile with resulting transfer of the fatty acyl group. At intracellular pH's this will require a powerful nucleophile and such reactions, when they occur, are known to occur preferential $\mathbf{1}$ y to a thiol acceptor (forming a thioester). the charged nature of the ammonium group, binding to the microsomal membranes and service there as a substrate for microsomal oxidases will not be favored and, thus, the only viable mechanism substance to react with the genetic material is the acyl transfer just mentioned, which for both compounds would involve essentially the same acyl transfer. Therefore, toxicity test of either one of these substances will be valid a predictor for the gene toxicity potential of the other.

8. One human skin irritation study was listed in the cover letter; a study of this type was submitted for PEQ analog CAS No. 68389-89-9 and PEQ CAS No. 68410-69-5.

Procter and Gamble did, indeed, submit human skin irritation studies on two PEQ compounds. This was done since:

- (a) Procter and Gamble has no human skin irritation studies of its own which are specific to EEQ CAS No. 68153-35-5 since this is not manufactured for fabric softeners;
- (b) Procter and Gamble wished to provide relevant information; and,
- (c) the PEQ analogs for which data was provided will accurately predict the skin irritation potential of EEQ.

This is because the structural differences between 68153-35-5 (see Figure 2) and 68389-89-9 (see Figure 2) or 68410-69-5 (see Figure 2) would not reasonably be expected to produce a different potential for skin irritation (in terms of potency or effects) for the PEQ compounds in comparison to EEQ. Since this is a physico-chemical property, and since these compounds have similar physico-chemical properties, these substances will all have similar skin irritation potential and a study of one is predictive of the others. After all, EEQ is in reality a homolog of PEQ in which the average number of ethoxy units in the polyethoxy chain is less than 1.5. "Pure" EEQ would of course have only one

ethoxy unit in the side chain. Thus, a distinction between commercial EEQ and PEQ is somewhat artificial in any case.

9. One human skin sensitization study was listed in the cover letter; a study of this type was submitted for PEQ analog CAS NO. 68389-89-9 and PEQ CAS No. 68410-69-5.

Procter and Gamble did, indeed, submit human skin sensitization studies on two PEQ compounds. This was done since:

- (a) Procter and Gamble has no human skin sensitization data of its own which is specific to EEQ CAS No. 68153-35-5 since this is not manufactured for fabric softeners;
- (b) Procter and Gamble wished to provide relevant information; and,
- the PEQs may be taken as reasonable analogs in regard to dermal sensitization potential since the mode of action, if any, would be acylation of protein material by the tallow amido groups found in both EEQ and PEQ (by trans-amidation to protein amino functional groups). Therefore, the analogs provided will give the same sensitization potential as will EEQ. The relevant structures are shown in Figure 2.
- 10. One acute bluegill toxicity study was listed in the cover letter; a study of this type was submitted for PEQ analog CAS No. 68389-89-9.

Procter and Gamble did, indeed, provide data on the aquatic toxicity to bluegill sunfish on a PEQ compound. This was done since:

- (a) Procter and Gamble has no aquatic toxicity data of its own which is specific to the effects of EEQ CAS No. 68153-35-5 on the bluegill sunsfish;
- (b) Procter and Gamble wished to provide relevant information; and,
- (c) the PEQ analog for which data was provided will accurately predict the aquatic toxicity of the EEO.

This is because the structural differences between 68153-35-5 (see Figure 2) and 68389-89-9 (see Figure 2) would not reasonably be expected to produce a different toxicity to fish (in terms of potency or effects) for the PEQ compounds in comparison to EEQ. After all, EEQ is in reality a homolog of PEQ in which the average number of ethoxy units in the polyethoxy chain is less than 1.5. "Pure" EEQ would of course have only one othoxy

unit in the side chain. Thus, a distinction between commercial EEQ and PEQ is somewhat artificial in any case.

As can be seen from Figure 2 both compounds have a nary center to which are attached two aminoalkyl group, a hydroxy alkyl group (this is a polyoxyethylene chain with an average number of ethoxyl units greater than 1.5 in the PEQs and with average number of ethoxyl units of 1.5 or less in EEQ). also has two tallow amide chains identically attached structure (to the nitrogen of the amino alkyl groups). These substances all be charged, bulky species with a strong surfactant/ detergent property. Such substances belong to a very broad class agents which exhibit toxicity to aquatic organisms by disrupting sensitive membranes which are required for oxygen and exchange between the organism and the surrounding water. membrane effects are driven by the physico-chemical properties of detergent / surfactant substances, and since EEQ and the PEQ analog have similar physico-chemical properties, both these substances will all have similar degrees of toxicity to aquatic organisms and a study of one will be predictive of the other.

11. One acute sheepshead minnow toxicity study was listed in the cover letter; a study of this type was submitted for PEQ analog CAS No. 68389-89-9.

Procter and Gamble did, indeed, provide data on the aquatic toxicity to sheepshead minnows on a PEQ compound. This was done since:

- (a) Procter and Gamble has no aquatic toxicity data of its own which is specific to the effects of EEQ CAS No. 68153-35-5 on the sheepshead minnows;
- (b) Procter and Gamble wished to provide relevant information; and,
- (c) the PEQ analog for which data was provided will accurately predict the aquatic toxicity of the EEQ.

This is because the structural differences between 68153-35-5 (see Figure 2) and 68389-89-9 (see Figure 2) would not reasonably be expected to produce a different toxicity to fish (in terms of potency or effects) for the PEQ compounds in comparison to EEQ. After all, EEQ is in reality a homolog of PEQ in which the average number of ethoxy units in the polyethoxy chain is less than 1.5. "Pure" EEQ would of course have only one ethoxy unit in the side chain. Thus, a distinction between commercial EEQ and PEQ is somewhat artificial in any case.

As can be seen from Figure 2 both compounds have a quaternary center to which are attached two aminoalkyl group, a hydroxy alkyl group (this is a polyoxyethylene chain with an average number of ethoxyl units greater than 1.5 in the PEQs and with an

average number of ethoxyl units of 1.5 or less in EEQ). Each structure also has two tallow amide chains identically attached (to the nitrogen of the amino alkyl groups). These substances will all be charged, bulky species with a strong surfactant/detergent property. Such substances belong to a very broad class of agents which exhibit toxicity to aquatic organisms by disrupting sensitive membranes which are required for oxygen and gas exchange between the organism and the surrounding water. These membrane effects are driven by the physico-chemical properties of detergent / surfactant substances, and since EEQ and the PEQ analog have similar physico-chemical properties, both these substances will all have similar degrees of toxicity to aquatic organisms and a study of one will be predictive of the other.

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12. One acute mysid shrimp toxicity study was listed in the cover letter; a study of this type was submitted for PEQ analog CAS No. 68389-89-9.

Procter and Gamble did, indeed, provide data on the aquatic toxicity to mysid shrimp on a PEQ compound. This was done since:

- (a) Procter and Gamble has no aquatic toxicity data of its own which is specific to the effects of EEQ CAS No. 68153-35-5 on mysid shrimp;
- (b) Procter and Gamble wished to provide relevant information; and,
- (c) the PEQ analog for which data was provided will accurately predict the aquatic toxicity of the EEQ.

This is because the structural differences between 68153-35-5 (see Figure 2) and 68389-89-9 (see Figure 2) would not reasonably be expected to produce a different aquatic invertebrate toxicity (in terms of potency or effects) for the PEQ compounds in comparison to EEQ. After all, EEQ is in reality a homolog of PEQ in which the average number of ethoxy units in the polyethoxy chain is less than 1.5. "Pure" EEQ would of course have only one ethoxy unit in the side chain. Thus, a distinction between commercial EEQ and PEQ is somewhat artificial in any case.

As can be seen from Figure 2 both compounds have a quater-nary center to which are attached two aminoalkyl group, a hydroxy alkyl group (this is a polyoxyethylene chain with an average number of ethoxyl units greater than 1.5 in the PEQs and with an average number of ethoxyl units of 1.5 or less in EEQ). Each structure also has two tallow amide chains identically attached (to the nitrogen of the amino alkyl groups). These substances will all be charged, bulky species with a strong surfactant/detergent property. Such substances belong to a very broad class of agents which exhibit toxicity to aquatic organisms by disrupting sensitive membranes which are required for oxygen and gas exchange between the organism and the surrounding water. These

membrane effects are driven by the physico-chemical properties of detergent _/ surfactant substances, and since EEQ and the PEQ analog have similar physico-chemical properties, both these substances will all have similar degrees of toxicity to aquatic organisms and a study of one will be predictive of the other.

13. One acute <u>Daphnia magna</u> toxicity study was listed in the cover letter; a study of this type was submitted for PEQ analog CAS No. 68389-89-9.

Procter and Gamble did, indeed, provide data on the aquatic toxicity to Daphnia on a PEQ compound. This was done since:

- (a) Procter and Gamble has no aquatic toxicity data of its own which is specific to the effects of EEQ CAS No. 68153-35-5 on Daphnia;
- (b) Procter and Gamble wished to provide relevant information; and,
- (c) the PEQ analog for which data was provided will accurately predict the aquatic toxicity of the EEQ.

This is because the structural differences between 68153-35-5 (see Figure 2) and 68389-89-9 (see Figure 2) would not reasonably be expected to produce a different aquatic invertebrate toxicity (in terms of potency or effects) for the PEQ compounds in comparison to EEQ. After all, EEQ is in reality a homolog of PEQ in which the average number of ethoxy units in the polyethoxy chain is less than 1.5. "Pure" EEQ would of course have only one ethoxy unit in the side chain. Thus, a distinction between commercial EEQ and PEQ is somewhat artificial in any case.

As can be seen from Figure 2 both compounds have a quaternary center to which are attached two aminoalkyl group, a hydroxy alkyl group (this is a polyoxyethylene chain with an average number of ethoxyl units greater than 1.5 in the PEQs and with an average number of ethoxyl units of 1.5 or less in EEQ). also has two tallow amide chains identically the nitrogen of the amino alkyl groups). These substances all be charged, bulky species with a strong surfactant/ detergent property. Such substances belong to a very broad class of agents which exhibit toxicity to aquatic organisms by disrupsensitive membranes which are required for oxygen and exchange between the organism and the surrounding water. These membrane effects are driven by the physico-chemical properties of detergent / surfactant substances, and since EEQ and the PEQ analog have similar physico-chemical properties, both these substances will all have similar degrees of toxicity to aquatic organisms and a study of one will be predictive of the other.

14. One freshwater algae toxicity study was listed in the cover letter; a study of this type was submitted for PEQ analog CAS No. 68389-89-9.

[Procter and Gamble did indeed provide data on the aquatic toxicity to freshwater algae of a PEQ compound. This was done since:

- (a) Procter and Gamble has no augatic toxicity data of its own which is specific to the effects of EEQ CAS No. 68153-35-5 on freshwater algae;
- (b) Procter and Gamble wished to provide relevant information; and,
- (c) the PEQ analog for which data was provided will accurately predict the aquatic toxicity of the EEQ.

This is because the structural differences between 68153-35-5 (see Figure 2) and 68389-89-9 (see Figure 2) would not reasonably be expected to produce a different toxicity to algae (in terms of potency or effects) for the PEQ compounds in comparison to EEQ. After all, EEQ is in reality a homolog of PEQ in which the average number of ethoxy units in the polyethoxy chain is less than 1.5. "Pure" EEQ would of course have only one ethoxy unit in the side chain. Thus, a distinction between commercial EEQ and PEQ is somewhat artificial in any case.

can be seen from Figure 2 both compounds have a quaternary center to which are attached two aminoalkyl group, a hydroxy alkyl group (this is a polyoxyethylene chain with an average number of ethoxyl units greater than 1.5 in the PEQs and with average number of ethoxyl units of 1.5 or less in EEQ). Each structure also has two tallow amide chains identically attached the nitrogen of the amino alkyl groups). These substances will all be charged, bulky species with a strong surfactant/ detergent property. Such substances belong to a very broad class of agents which exhibit toxicity to algae by disrupting sensitive membranes which are required for metabolic processes exchange between the algae and the surrounding water. These membrane effects are driven by the physico-chemical properties of detergent / surfactant substances, and since EEQ and the PEQ analog have similar physico-chemical properties, both these substances will all have similar degrees of toxicity to freshwater algae and a study of one will be predictive of the other.

Procter and Gamble Tests on Varisoft 475

The purpose of the referenced 91 day percutaneous toxicity study in rabbits was to examine the toxicity potential of Varisoft 475 (which is 75% to 90% IQAC [CAS No. 68122-86-1] in isopropanol using a test article in which the dermal irritancy of undiluted Varisoft 475 would not be the limiting factor for the test. We believe that the NOEL which was reported in the Committee's summary document on quaternary ammonium compounds was calculated on the IQAC content basis.

Similarly, the PEQ study which is noted in the ITC letter was designed to allow for subchronic repeated dermal application of a test article which is irritant to the skin in undiluted form. The NOEL which was reported in the previously submitted summary document was, we believe, based on the PEQ content of the applied test article.

Figure 1: IQAC Compounds

CAS# 68122-86-1 Imidazolium compounds, 4,5-Dihydro-1-methyl-2-nortallow alkyl-1-(2-tallow amidoethyl), Methyl sulfates

CAS# 72623-82-6 Imidazolium compounds, 2-(C_{13} - C_{17} alkyl)-1-[2-(C_{14} - C_{18} amidoethyl)-4,5-dihydro-3-methyl, Methyl sulfates

Figure 2: PEQ Compounds and EEQ Compounds

CAS# 68410-69-5 Poly (oxy-1,2-ethanediyl), α -[2-[bis (2-aminoethyl) methylammonio] ethyl]- ω -hydroxy-N,N'-ditallow acyl derivs., Me sulfate (salts)

CAS# 68389-89-9 Poly (oxy-1,2-ethanediyl), α -[2-[bis (2-aminoethyl) methylammonio] ethyl]- δ -hydroxy-N,N'-bis (hydrogenated tallow acyl) derivs., Me sulfate (salts)

CAS# 68413-04-7 Poly [oxy(methyl-1,2-ethanediyl)], α -[2-[bis (2-aminoethyl) methylammonio] methylethyl]- ω -hydroxy-N,N'-ditallow acyl derivs., Me sulfate (salts)

CAS# 68153-35-5 Ethanaminium, 2-amino-N-(2-aminoethyl)-N-(2-hydroxyethyl)-N-methyl, N,N'-ditallow acyl derivs., Me sulfate (salts)

For CAS# 68410-69-5:

R = tallow

R' = Poly (oxy-1,2-ethanediy!)

For CAS# 68389-89-9:

R = hydrogenated tallow

R' = Poly (oxy-1, 2-ethanediyl)

For CAS# 68413-04-7:

R = tallow

R' = Poly [oxy (methyl-1,2-ethanediyl)]

For CAS# 68153-35-5:

R = tallow

R' = 2-hydroxyethyl

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Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

Attachment 1:

Report to Culver Chemical Company - Acute Oral Toxicity Study on Culversoft S-75 in Albino Rats [IQAC 68122-86-1]

REPORT TO

CULVER CHEMICAL COMPANY

ACUTE ORAL TOXICITY STUDY ON CULVERSOFT S-75 IN ALBINO RATS

IBT NO. A8214.

I. Introduction

At the request of Culver Chemical Company an acute oral toxicity study was conducted on a yellow liquid identified as Culversoft S-75,/75 Lot No. 180636. The sample was shaken well immediately prior to use.

NOTE:

Please be advised that as of July 1, 1970, Northern Petrochemical Co. purchased Culver Chemical Co.

The name Culversoft S-75 was changed to Varisoft 475.

II. Summary -

An acute oral toxicity study was conducted on Culversoft S-75, Lot No. 180636. The test material was evaluated as is at dose levels of 10.2, 15.4, 23.1 and 34.6 g/kg. Four albino rats (two males and two females) were tested at each level. None of the animals dosed at the lower two levels died while three rats in the 23.1 g/kg group and all four animals in the 34.6 g/kg group died. The acute oral median lethal dose (LD50) ± the standard deviation was calculated to be 20.8 ± 2.1 g/kg. General signs of intoxication included the following: hypoactivity, ataxia, muscular weakness, diarrhea, prostration, and a ruffed fur. Necropsy of the animals that died revealed gastroenteritis. No gross pathologic alterations were noted among the animals sacrificed at the end of the observation period.

Respectfully submitted,

INDUSTRIAL BIO-TEST LABORATORIES, FINC.

Report prepared by:

Carmen Mastri, B.S.

Section Head

Acute Toxicity Department

Report approved by:

M. L. Keplinger, Ph.D.

Manager, Toxicology

Otis E. Fancher, Ph.D.

Director

III. Procedure

Healthy, young albino rats of the Charles River strain (COBS)* ranging in body weight from 150 to 200 grams were used as test animals. All animals used were kept under observation for five days prior to experimental use, during which period they were checked for general physical health and suitability as test animals. The animals were housed in stock cages and permitted a standard laboratory rat diet** plus water ad libitum until 16 hours immediately prior to oral intubation.

Initial screening was conducted in order to determine the general level of toxicity and then selected groups of four rats each (two male and two female) were intubated with previously calculated doses of the undiluted test material. All doses were administered directly into the stomachs of the rats using a hypodermic syringe equipped with a ball-pointed intubating needle.

Following oral administration of the test material, the rats were housed individually in observation cages (10" x 8" x 8") and observed for the succeeding 14 days. Initial and final body weights as well as all mortalities—and/or reactions displayed were recorded. Arrangements were made to autopsy any animal which might succumb during the study as well as all surviving animals at the end of the 14 days.

^{*} Charles River Breeding Laboratories, Inc., North Wilmington, Massachusetts.

^{##} Purina Rat Chow, Ralston Purina Company, St. Louis, Missouri.

At the end of the observation period, all data were collected and arrangements were made to calculate, if possible, the acute oral median lethal dose (LD50) of the test material using the techniques of Weil*, Thompson**, and Thompson and Weil***.

^{*} Weil, Carrol S.: Tables for Convenient Calculation of Median-Effective Dose (LD₅₀ or ED₅₀) and Instructions in Their Use. <u>Biometrics</u>, Sept. 1952.

^{**} Thompson, William R.: Use of Moving Averages and Interpolation, to Estimate Median-Effective Dose. <u>Bact. Rev.</u>, Nov. 1947.

^{***} Thompson, William R. and Weil, Carrol S.: On the Construction of Tables for Moving Average Interpolation. <u>Biometrics</u>, March 1952.

IV. Results

A. Mortality and Body Weights

Individual mortality and body weight data are presented in Table I.

TABLE I

TEST MATERIAL: Culversoft S-75

Acute Oral Toxicity Study - Albino Rats

Mortality and Body Weight Data

| | Animal I | ndividual Boo | ly Weights (grams) |) | |
|--------|-----------|---------------|--------------------|---------------|----------|
| Dose* | Number | Test Day | Number: | Number Dead | Percent |
| (g/kg) | and Sex 4 | 0 | 14 | Number Tested | Dead |
| 10.2 | 1-M | 206 | 308 | 0/4 | 0 |
| | 2-M | 208 | 314 | -, - | |
| | 3-F | 212 | . 236 | | |
| | 4-F | 214 | 250 | | |
| 15,4 | 5-M | 204 | 298 | 0/4 | 0 |
| | 6-M | 182 | 264 | | • |
| | 7-F | 196 | 222 | | |
| | 8-F | 197 | 216 | | |
| 23. 1 | 9-M | 171 | 255 | 3/4 | 75 |
| | 10-M | 177 | (2 days) | | , , |
| | 11-F | 152 | (2 days) | | |
| | 12-F | 158 | (5 days) | | |
| 34.6 | 13-M | 180 | (2 days) | 4/4 | - 100 |
| | 14-M | 165 | (3 days) | • | |
| | 15-F | 170 | (2 days) | | |
| | 16-F | 152 | (4 days) | | #100 |

Note: Figures in parentheses indicate time of death.

Acute Oral LD50 = 20.8 g/kg Standard Deviation of LD50 = ± 2.1 g/kg

^{*} Culversoft S-75 was administered as is.

B. Reactions

The reactions exhibited by the animals following oral administration of Culversoft S-75 are presented in Table II.

Necropsy of the animals that died revealed gastroenteritis. No gross pathologic alterations were noted among any of the animals sacrificed at the end of the 14-day observation period.

TABLE II

TEST MATERIAL: Culversoft S-75

Acute Oral Toxicity Study - Albino Rats

Summary of Reactions

| Dose (د/برو) | Reaction | Time of Onset Following Dose' Administration (hours) | Duration of of Reaction (days) | Time of Death Following Dose Administration (days) |
|-----------------|--|---|--------------------------------|---|
| 10.2 | Hypoactivity Ruffed fur | 1/2 6-22 | 1 2 | 1 |
| 15.4 | Hypoacti vity Ruffed fur Muscular weakness Diarrhea | 1/2 6-22 6-22 6-22 | .๓ พ พ พ | |
| 23.1 | Hypoactivity Ataxia Muscular weakness Prostration Diarrhea Ruffed fur | 1/2 1 1 5 6-22 6-22 | 5 6-22 hours 2 2 2 | 2-5 |
| 34.6 | Hypoactivity Ataxia Muscular weakness Prostration Diarrhea Ruffed fur | 1/2 1/2 1 1 1 6-22 6-22 | Until death | 2-4 |

3

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Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

Attachment 2:

Toxicity Studies for Ashland Oil Company [IQAC 68122-86-1, misc. formulations]

*TOXICITY STUDIES

FOR

ASHLAND OIL COMPANY

COMPILED BY: M. Patricia Prate

⟨EPORTED:
December 18, 1973

Bio-Toxicology Laboratories, Inc.

Twin Oak Farm Division Creek & Cox Roads, P. O. Box 267, Moorestown, N. J. 08057 Phone: (609) 665-1776 — 235-2908

December 18, 1973

Dr. N.S. Salomons Ashland Oil, Inc. 5200 Blazer Parkway Dublin, Ohio 43017

Dear Dr. Salomons:

Following are the results of the experimental procedures conducted for Ashland Oil, Inc.

MATERIAL:

Varisoft 475 Varisoft 475 (5% free amine) Varisoft 475

(13.5 wt. % solids)

Varisoft 475

(13.5 wt. % solids -

5% free amine)

RECEIVED:

November 21, 1973

EXPERIMENTAL PERIOD:

November 26 - December 18, 1973

EXPERIMENTAL PROCEDURES:

Eye Irritation Study Primary Irritation Study Acute Oral LD50 Study

The conclusions in this study are based upon the results of the study completed December 18, 1973.

This report is submitted for the exclusive use of Ashland Oil, Inc.

JDP/1sd

Very truly yours,

President

EYE IRRITATION STUDY

Federal Hazardous Substances Labeling Act

Varisoft 475 (13.5 wt.% solids)
Varisoft 475 (13.5 wt.% solids -5% free amine)

DRAIZE RABBIT EYE IRRITATION STUDY PROCEDURE FEDERAL HAZARDOUS SUBSTANCES LABELING ACT

A group of 12 albino rabbits was used in this study to determine the toxicity of the substances submitted to eye mucosa. A series of 6 rabbits was used for testing each substance.

One tenth of a milliliter of the product under test was instilled into the conjunctival sacs of the test animals. All treated eyes were unwashed. Ocular evaluations were made with the unaided eye. These evaluations were made at 24, 48 and 72 hours.

The cornea is scored on the basis of the density of the opacity and the total area involved. The iris is scored on the intensity or degree of inflammation exhibited; and the palpebral and bulbar mucosae are scored on the extent of chemosis, hyperemia and discharge.

DRAIZE SCALE FOR SCORING OCULAR LESIONS

| | | TOTAL GOODER LESIONS |
|----|------|--|
| 1. | Cor | nea - |
| | Α. | Opacity-Degree of Density (area which is most dense taken for reading) |
| | | Scattered or diffuse area-details of iris clearly visible |
| | | Opalescent areas, no details of iris visible size of |
| | | public barely discernible |
| | ъ | The state of the s |
| | В. | and of Corneal dalilade Involved |
| | | One quarter of area (or less) but not zero |
| | | |
| | | crosto: man one half, less than three quarters |
| | | |
| 2. | Iris | Score equals A x B x 5 Total maximum - 80 |
| -• | Α. | Values |
| | | |
| | | Folds above normal, congestion, swelling circumcorneal injection (any one or all of these or combination of any thereof), iris |
| | | still reaction to light, (sluggish reaction is positive) |
| | | 110 1000 to light, nemorrhage; gross destruction / |
| | | one of all of these) |
| | | Score equals A x 5 Total possible maximum - 10 |
| 3. | Conj | unctivae |
| | A. | Redness (refers to palpebral and bulbar conjunctivae excluding |
| | | cornea and mis) |
| | | Vessels definitely injected above normal |
| | | arruse, deeper chimson red, individual vascals, not |
| | | easily discernible |
| | В. | Diffuse beefy red |
| | | Any swelling above normal (includes nictitating membrane) |
| | | Obvious swelling with partial eversion of the lids |
| | | swerring with hids about half closed |
| | _ | swelling with hids about half closed to completely closed |
| | C. | 215Charge |
| | | Any amount different from normal (does not include small amount |
| | | observed in inner canthus of normal animals) |
| | | Discharge with moistening of the lids and hairs just adjagant |
| | | to the lids |
| | | around eye |
| | | Score $(A + B + C) \times 2$ Total maximum - 20 |
| | | The maximum total score is the sum of all scores obtained for the cornea, |
| | | iris and conjunctivae. Total maximum score possible - 110 points |

BASIS OF CLASSIFICATION AND CONCLUSIONS

The following arbitrary designation of classification is offered as a guide in judging the severity of a compound when subjected to the Draize Eye Irritation Technique. This classification is subject to immediate revision upon suggestion or directive, from municipal or federal governmental agencies.

Conclusions in this report are based upon the particular samples and animals employed, temperature variants, and other conditions controllable or uncontrollable by the physicians, veterinarians, technicians, operators, observers and compilators of this study and report.

CLASSIFICATION KEY

- O = duration and magnitude of irritation, comparable to distilled water
- I = mild irritant (total points scored/day less than 10; no score under cornea or iris)
- II = moderate irritant (total points scored/day less than 15; no score under cornea or iris)
- III = strong irritant (total points scored/day 15 or more; no score under cornea
 iris)

SUB-GROUPINGS

- A = short duration (zero score on or before third day)
- B = moderate duration (zero score by fourth or fifth day)
- C = long duration (zero score by sixth or seventh day)
- D = prolonged duration (score on seventh day)
- E = temporary corneal or iris lesions (not apparent on seventh day)
- F = permanent corneal or iris lesions (continuing past seventh day)

Example: III A to III DF --- indicates compound is a strong irritant of short to prolonged duration, capable of producing permanent corneal or iris lesions, when instilled into the eyes of albino rabbits.

SCORE SHEET

Varisoft 475 (13.5 wt. % solids)
Varisoft 475 (13.5 wt. % solids - 5% free amine)

Product Tested

Varisoft 475

(13.5 wt.% solids)

Animal No.

1 Unwashed

| Hours | 24 | 48 | 72 |
|--------------------------------------|----|----|----|
| I- CORNEA | | | |
| A- Opacity | | | |
| B- Area Involved | | | |
| II- IRIS | | | |
| A- Evaluation | | | |
| III- CONJUNCTIVAE | | | - |
| A- Hyperemia | 1 | | |
| B- Chemosis | | | • |
| C- Discharge | | | |
| Total Points (Total Possible 110) | 2 | | |

NOTE: ABSENCE OF NUMERICAL SCORING INDICATES SCORES = 0

Classification: I.A.

Product Tested

Varisoft 475

(13.5 wt.% solids)

Animal No.

2 Unwashed

| Hours | 24. | 48 | 72 |
|--------------------------------------|-----|----|----|
| I- CORNEA | | | |
| A- Opacity | | | ! |
| B- Area Involved | | | |
| II- IRIS | | | · |
| A- Evaluation | | | |
| III- CONJUNCTIVAE | | | |
| A- Hyperemia | 1 | 1 | |
| B- Chemosis | | | |
| C- Discharge | | | |
| Total Points (Total Possible 110) | 2 | 2 | |
| | | | |

NOTE: ABSENCE OF NUMERICAL SCORING INDICATES SCORES = 0
Classification: I.A.

Product Tested

Varisoft 475

(13.5 wt.% solids)

Animal No.

3 Unwashed

| Hours | 24 | 48 | 72 |
|--------------------------------------|----|----|----|
| I- CORNEA | | | |
| A- Opacity | | | |
| B- Area Involved | | | |
| II- IRIS | | | |
| A- Evaluation | | | |
| III- CONJUNCTIVAE | | | |
| A- Hyperemia | 1 | | |
| B- Chemosis | | | |
| C- Discharge | | | |
| Total Points (Total Possible 110) | 2 | | |

NOTE: ABSENCE OF NUMERICAL SCORING INDICATES SCORES = 0

Classification: I.A.

Product Tested

Varisoft 475

(13.5 wt. % solids)

inimal No.

4 Unwashed

| Hours | 24 | 48 | 72 |
|-----------------------------------|----|----|----------|
| I- CORNEA | | | |
| A- Opacity | | | |
| B- Area Involved | | | |
| Π- IRIS | | | <u> </u> |
| A- Evaluation | | | |
| III- CONJUNCTIVAE | | | • |
| A- Hyperemia | 1 | I | |
| B- Chemosis | | | |
| C- Discharge | | | |
| Total Points (Total Possible 110) | 2 | 2 | |

NOTE: ABSENCE OF NUMERICAL SCORING INDICATES SCORES = 0 Classification: I.A.

Product Tested

Varisoft 475

(13.5 wt. % Solids)

Animal No.

5 Unwashed

| Hours | 24 | 48 | 72 |
|--------------------------------------|----|--------------|----|
| I- CORNEA | | | |
| A- Opacity | | | |
| B- Area Involved | | | |
| Π- IRIS | | * | |
| A- Evaluation | | | |
| III- CONJUNCTIVAE | | <u> </u> | |
| A- Hyperemia | 1 | | Α, |
| B- Chemosis | | | |
| C- Discharge | | | |
| Total Points (Total Possible 110) | 2 | | |

NOTE: ABSENCE OF NUMERICAL SCORING INDICATES SCORES = 0 Classification: I.A.

coduct Tested

Varisoft 475

(13.5 wt. % Solids)

nimal No.

6 Unwashed

| | | | , |
|--------------------------------------|----|----|----|
| Hours | 24 | 48 | 72 |
| I- CORNEA | | | |
| A- Opacity | | | |
| B- Area Involved | | | |
| Π- IRIS | | | |
| A- Evaluation | | | |
| III- CONJUNCTIVAE | | | |
| A- Hyperemia | 1 | | |
| B- Chemosis | | | |
| C- Discharge | | | |
| Total Points (Total Possible 110) | 2 | | |

NOTE: ABSENCE OF NUMERICAL SCORING INDICATES SCORES = 0

Classification: I.A.

Product Tested

Varisoft 475

(13.5 wt. % solids -

5% free amine)

Animal No.

1 Unwashed

| | T | , | |
|--------------------------------------|----|---|---------------------------------------|
| Hours | 24 | 48 | 72 |
| I- CORNEA | | | |
| A- Opacity | | | |
| B- Area Involved | | | |
| Π- IRIS | | | |
| A- Evaluation | | | · · · · · · · · · · · · · · · · · · · |
| II- CONJUNCTIVAE | | | |
| A- Hyperemia | 1 | | |
| B- Chemosis | | | |
| C- Discharge | | | |
| Total Points (Total Possible 110) | 2 | | |

NOTE: ABSENCE OF NUMERICAL SCORING INDICATES SCORES = 0

Classification: I.A.

Varisoft 475
(13.5 wt.% solids 5% free amine)

2 Unwashed

| Hours | 24 | 48 | 72 |
|--------------------------------------|----|----|----|
| I- CORNEA | | | |
| A- Opacity | | | |
| B- Area Involved | | | |
| Π- IRIS | | | |
| A- Evaluation | | | |
| III- CONJUNCTIVAE | | | |
| A- Hyperemia | 1 | | |
| B- Chemosis | | | |
| C- Discharge | | | |
| Total Points (Total Possible 110) | 2 | | |

ABSENCE OF NUMERICAL SCORING INDICATES SCORES = 0

fic tion: I.A.

Product Tested

Varisoft 475

(13.5 wt. % solids -

5% free amine)

Animal No.

3 Unwashed

| Hours | 24 | 48 | 72 |
|--------------------------------------|----|----|----|
| I- CORNEA | | | |
| A- Opacity | | | |
| B- Area Involved | | | |
| Π- IRIS | | , | |
| A- Evaluation | | | |
| III- CONJUNCTIVAE | | | |
| A- Hyperemia | 1 | 1 | |
| B- Chemosis | | | |
| C- Discharge | | | |
| Total Points (Total Possible 110) | 2 | 2 | |

NOTE: ABSENCE OF NUMERICAL SCORING INDICATES SCORES = 0

Classification: I.A.

Product Tested

Varisoft 475

(13.5 wt. % solids -

\$% free amine)

Animal No.

4 Unwashed

| Hours | 24 | 48 | 72 |
|-----------------------------------|----|----|----|
| I- CORNEA | | | |
| A- Opacity | | | |
| B- Area Involved | | | |
| Π- IRIS | | , | |
| A- Evaluation | | | |
| III- CONJUNCTIVAE | | | |
| A- Hyperemia | 1 | 1 | |
| B- Chemosis | | | |
| C- Discharge | | | |
| Total Points (Total Possible 110) | 2 | 2 | |

NOTE: ABSENCE OF NUMERICAL SCORING INDICATES SCORES = 0
Classification: I.A.

SUMMARY OF POINTS SCORED

Varisoft 475 (13.5 wt. % solids)
Varisoft 475 (13.5 wt.% solids - 5% free amine)

SUMMARY OF POINTS SCORED

| | | | | | | | | | |
|---------------|---------|--------------|-------|-----|------|------|--|--------|---|
| | - | Total Points | 16 | 18 | | | | | |
| | nds | 3 | | | | | | | |
| EYES | seconds | 2 | | | | | | | |
| E | 11 | | | | | | | | |
| WASHED | M A A | 3 | | | | | | | |
| WAS | N I M | 2 | | | | | | | |
| _ | A 2 | • | | | | | | | |
| _ | | | | | | | | - | |
| = | | | | | | | | | |
| | | 6 | . 2 | 2 | | | | | |
| ES | ## | 5 6 | 2 2 | 4 2 | | | | | - |
| EYES | 1 | | | | | | | ÷ | - |
| - 1 | 1 | 2 | 2 | 4 | | | | ÷ | - |
| - 1 | 1 | 4 5 | 4 | 4 | | | | à" 🔪 . | - |
| UNWASHED EYES | 1 | 3 4 5 | 2 4 2 | 4 4 | | | | ÷ | - |

Bio-Toxicology Laboratories • Toxicity and Applied Research Studies - Animal and Human

Department of Transportation Act

Varisoft 475 Varisoft 475 (5% Free Amine) Varisoft 475 (13.5 wt. % Solids) Varisoft 475 (13.5 wt. % Solids - 5% Free Amine)

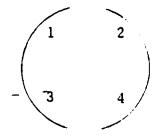
METHOD FOR PRIMARY IRRITATION

DEPARTMENT OF TRANSPORTATION ACT

The intact and abraded skin of 24 albino rabbits was employed for this study. A series of 6 rabbits was used for testing each substance. The hair was clipped from the backs with the aid of angora clippers. Four areas of the back, placed approximately ten centimeters apart, were designated for the positions of the patches. Areas 2 and 3 were abraded by making four epidermal incisions (two perpendicular to two others in the area of the patch). The patches consisted of 1.5 inch x 1.5 inch 12 ply gauze squares. The patches were secured to the area by thin bands of adhesive tape. The material to be tested (0.5 ml. for liquids and 0.5 gm. for solids) was introduced beneath the patch. The entire trunks of the animals were then wrapped in clear plastic trunk bands. The trunk bands help to hold the patches in position and retard evaporation of volatile substances during the four hour exposure period. Upon removal of the patches the resulting reactions were evaluated on the basis of weighted scores.

Following this initial reading, all test sites were washed with appropriate solvent to prevent further exposure. Readings were again made at 24 and 48 hours after the initial application. Each test substance is evaluated on a total of site (6 abraded and 6 intact).

The primary irritation index is calculated by adding the values for erythema or eschar formation, and edema at 4, 24 and 48 hours on intact and abraded skin (12 values) and dividing by six to obtain an individual score on each rabbit.



2 and 3 = abraded

1 and 4 = intact

1 and 2 = control (if employed)

3 and 4 = test material

METHOD OF POINT SCORING

FOR

EVALUATION OF SKIN REACTIONS

| A. | Erythema and Eschar Formation | |
|-------|--|----------------|
| | Very slight erythema (barely perceptible) | 1 |
| | Well defined erythema | 2 |
| | Moderate to severe erythema Severe erythema (beet redness) to slight eschar formation | 3 |
| | (injuries in depth) | 4 |
| | Total possible erythema score | 4 |
| В. | Edema Formation | |
| | Very slight edema (barely perceptible) | 1 |
| | Slight edema (edges of area well defined by definite raising) | 2 |
| | Moderate edema (area raised approximately 1 mm.) | 3 |
| | Severe edema (raised more than 1 mm. and extending beyond | |
| | area of exposure) | 4 |
| | Total possible edema score | 4 |
| | Total possible score for primary irritation | - 8 |
| | or sensitization | 8 |
| | * | |
| | | |
| Prima | ary Irritation Index Sensitization | |
| 2 - | lessmild irritant 2 or lessmild sensitiz | zer Isitizi |

6 or above.....severe irritant

6 or above.....severe sensitizer

SCORE SHEETS

Varisoft 475
Varisoft 475 (5% free amine)
Varisoft 475 (13.5 wt.% solids)
Varisoft 475 (13.5 wt. % solids - 5% free amine)

Product Tested: Varisoft 475

| | | | ythema-esc observation | | Ede | ma observa | ition | |
|---------|-----------|-------|---------------------------|--------|-------|------------|--------|---------|
| RABBIT# | SKIN | 4 hr. | 24 hr. | 48 hr. | 4 hr. | 24 hr. | 48 hr. | AVERAGE |
| 1 | Intact | 1 | 1 | 0 | 0 | 0 | 0 | 0.83 |
| | Abraded , | 2 | 1 | 0 | 0 | 0 | 0 - | |
| 2 | Intact | 1 | 0 | 0 | 0 | 0 | 0 | 0.50 |
| | Abraded | 1 | 1 | 0 | 0 | 0 | 0 | |
| 3 | Intact | 1 | 1 | 0 | 0 | 0 | 0 | 0.66 |
| | Abraded | 1 | 1 | 0 | 0 | 0 | 0 | |
| 4 | Intact | 1 | 0 | 0 | 0 | 0 | 0 | 0.83 |
| | Abraded | 2 | 1 | 1 | 0 | 0 | 0 | |
| 5 | intact | 1 | 1 | 0 | 0 | 0 | 0 | 0.83 |
| | Abraded | 2 | 1 | 0 | 0 | 0 | 0 | • |
| 6 | Intact | 1 | 1 | 0 | 0 | 0 | 0 | 1.16 |
| | Abraded | 2 | 2 | 1 | 0 | 0 | 0 | |

PRIMARY IRRITATION INDEX OF COMPOUND 0.8 (mild primary irritant)

| | Evaluation of | Ratio regarding six rabbits Observation time | | | | |
|-----------|---------------|--|---------|---------|--|--|
| Test Site | Skin Reaction | 4 hrs. | 24 hrs. | 48 hrs. | | |
| Intact | Non-Corrosive | 6:6 | 6:6 | 6:6 | | |
| Abraded | Non-Corrosive | 6:6 | 6:6 | 6:6 | | |

Product Tested: Varisoft 475 (5% Free Amine)

| | | ythema-eso | | Ede | ma observa | ation | |
|-----------|--|--|---|--|---|---|---|
| SKIN | 4 hr. | 24 hr. | 48 hr. | 4 hr. | 24 hr. | 48 hr. | AVERAGE |
| Intact | 1 | 1 | 1 | 0 | | 0 | 1.83 |
| Abraded * | 2 | 2 | 1 | 0 | 1 | 1 | |
| Intact | 1 | 1 | 0 | 0 | 0 | 0 | 2.00 |
| Abraded | 3 | 2 | 2 | 0 | 2 | 1 | |
| Intact | 1 | 0 | 0 | 0 | 0 | 0 | 1.00 |
| Abraded | 2 | 1 | 1 | 0 | 1 | 0 | |
| Intact | 1 | 1 | 0 | 0 | 0 | 0 | 1.83 |
| Abraded | 2 | 2 | 2 | 0 | 2 | 1 | |
| Intact | 1 . | 1 | 1 | 0 | 0 | 0 | 1.66 |
| Abraded | 3 | 2 | 1 | 0 | 1 | 0 | - |
| Intact | 1 | 0 | 0 | 0 | 0 | 1 | 1.66 |
| Abraded | 2 | 2 | 1 | 0 | 2 | 1 | 21 X 11 |
| | Intact Abraded Intact Abraded Intact Abraded Intact Abraded Intact Abraded Intact Abraded Intact | SKIN 4 hr. Intact 1 Abraded 2 Intact 1 Abraded 3 Intact 1 Abraded 2 Intact 1 Abraded 2 Intact 1 Abraded 3 Intact 1 Abraded 3 Intact 1 | SKIN 4 hr. 24 hr. Intact 1 1 Abraded 2 2 Intact 1 1 Abraded 3 2 Intact 1 0 Abraded 2 1 Intact 1 1 Abraded 2 2 Intact 1 1 Abraded 3 2 Intact 1 0 | Observation SKIN 4 hr. 24 hr. 48 hr. Intact 1 1 1 Abraded 2 2 1 Intact 1 1 0 Abraded 3 2 2 Intact 1 0 0 Abraded 2 1 1 Intact 1 1 0 Abraded 2 2 2 Intact 1 1 1 Abraded 3 2 1 Intact 1 0 0 | Observation Ede SKIN 4 hr. 24 hr. 48 hr. 4 hr. Intact 1 1 1 0 Abraded 2 2 1 0 Intact 1 1 0 0 Abraded 2 1 1 0 Intact 1 1 0 0 Abraded 2 2 2 0 Intact 1 1 1 0 Abraded 3 2 1 0 Intact 1 0 0 0 | SKIN Edema observation Intact 1 1 1 0 0 Abraded 2 2 1 0 0 Abraded 3 2 2 0 2 Intact 1 0 0 0 0 Abraded 2 1 1 0 0 0 Abraded 2 1 1 0 0 0 0 Abraded 2 2 2 0 2 1 1 0< | SKIN 4 hr. 24 hr. 48 hr. 4 hr. 24 hr. 48 hr. Intact 1 1 1 0 0 0 Abraded 2 2 1 0 1 1 Intact 1 1 0 0 0 0 Abraded 3 2 2 0 2 1 Intact 1 0 0 0 0 0 Abraded 2 1 1 0 0 0 0 Abraded 2 2 2 0 2 1 Intact 1 1 1 0 0 0 0 Abraded 3 2 1 0 0 0 0 Abraded 3 2 1 0 0 0 0 Intact 1 0 0 0 0 1 0 |

| - | Evaluation of | | regarding six Observation tir | |
|-----------|---------------|--------|----------------------------------|---------|
| Test Site | Skin Reaction | 4 hrs. | 24 hrs. | 48 hrs. |
| Intact | Non-Corrosive | 6:6 | 6:6 | 6:6 |
| Abraded | Non-Corrosive | 6:6 | 6:6 | 6:6 |

Product Tested: Varisoft 475

(13.5 wt. % solids)

| | | | ythema-eso observation | | Ede | ma observ | ation | |
|---------|---------|-------|---------------------------|--------|-------|-----------|--------|----------------|
| RABBIT# | SKIN | 4 hr. | 24 hr. | 48 hr. | 4 hr. | 24 hr. | 48 hr. | AVERAGE |
| 1 | Intact | 1 | 1 | 0 | 0 | 0 . | 0 | 0.66 |
| | Abraded | Į. | 1 | 0 | 0 | 0 | 0 | |
| 2 | Intact | 1 | 0 | 0 | 0 | 0 | 0 | 0.50 |
| | Abraded | 1 | 1 | 0 | 0 | 0 | 0 | |
| 3 | Intact | 0 | 0 | 0 | 0 | 0 | 0 | 0.50 |
| | Abraded | 1 | 1 | 1 | 0 | 0 | 0 | |
| 4 | Intact | 1 | 1 | 1 | 0 | 0 | 0 | 1.00 |
| | Abraded | 1 | 1 | 1 | 0 | 0 | 0 | |
| 5 | Intact | 0 | . 0 | 0 | 0 | 0 | 0 | 0.33 |
| | Abraded | 1 | 1 | 0 | 0 | 0 | 0 | - |
| 6 | Intact | 1 | 0 | 0 | 0 | 0 | 0 | 0.66 |
| | Abraded | 1 | 1 | 1 | 0 | 0 | 0 | ** * ** |

PRIMARY IRRITATION INDEX OF COMPOUND

0.6 (mild primary irritant)

| | Evaluation of | 1 | o regarding six Observation tir | |
|-----------|---------------|--------|------------------------------------|---------|
| Test Site | Skin Reaction | 4 hrs. | 24 hrs. | 48 hrs. |
| intact | Non-Corrosive | 6:6 | 6:6 | 6:6 |
| Abraded | Non-Corrosive | 6:6 | 6:6 | 6:6 |

Product Tested: Varisoft 475

(13.5 wt. % solids 5% Free Amine)

| | | | ythema-eso observation | | Ede | ma observa | ation | |
|---------|---------|------------|---------------------------|--------|-------|------------|--------|---------------|
| RABBIT# | SKIN | 4 hr. | 24 hr. | 48 hr. | 4 hr. | 24 hr. | 48 hr. | AVERAGE |
| 1 | Intact | 1 | 1 | 0 | 0 | 0 | 0 | 1.33 |
| | Abraded | € 2 | 1 | 1 | 0 | 1 | 1 | 1.00 |
| 2 | Intact | 1 | 1 | 0 | 0 | 0 | 0 | 1.50 |
| | Abraded | 2 | 2 | 1 | 0 | 1 | 1 | |
| 3 | Intact | 1 | 1 | 0 | 0 | 0 | 0 | 1.66 |
| | Abraded | 2 | 2 | 1 | 0 | 2 | 1 | |
| 4 | Intact | 1 | 1 | 0 | 0 | 0 | 0 | 1.50 |
| | Abraded | 2 . | 2 | 1 | 0 | 1 | 1 | |
| 5 | Intact | 1 | . 0 | 0 | 0 | 0 | 0 | 0.83 |
| , | Abraded | 1 | 1 | 1 | 0 | 1 | 0 | • |
| 6 | Intact | 1 | 1 | 0 | 0 | 0 | 0 | 1.17 |
| | Abraded | 2 | 1 | 1 | 0 | 1 | 0 | 40 40 × 50 |

| | Evaluation of | Ratio regarding six rabbits Observation time | | | | |
|-----------|---------------|--|---------|---------|--|--|
| Test Site | Skin Reaction | 4 hrs. | 24 hrs. | 48 hrs. | | |
| Intact | Non-Corrosive | 6:6 | 6:6 | 6:6 | | |
| Abraded | Non-Corrosive | 6:6 | 6:6 | 6:6 | | |

Federal Hazardous Substances Labeling Act

Varisoft 475

Varisoft 475 (5% Free Amine)

Varisoft 475 (13.5 wt. % Solids)

Varisoft 475 (13.5 wt. % Solids - 5% Free Amine)

METHOD FOR PRIMARY IRRITATION-RABBIT SKIN FEDERAL HAZARDOUS SUBSTANCES LABELING ACT

The intact and abraded skin of 24 albino rabbits was used for this study. A series of 6 rabbits was used for testing each substance. The hair was clipped from the backs with the aid of angora clippers. Two areas of the back, placed approximately ten centimeters apart, were designated for the positions of the patches. One area was abraded by making four epidermal incisions (two perpendicular to two others in the area of the patch.) The patches consisted of two layers of light gauze cut in squares (2.5 cm. on the side). The patches were secured to the area by thin bands of adhesive tape. The material to be tested (0.5 ml.) was introduced beneath the patch. The entire trunks of the animals were then wrapped in clear plastic trunk bands. The trunk bands help to hold the patches in position and retards evaporation of volatile substances during the twenty-four hour exposure. The compound under test was applied so that there were two applications (one intact and one abraded) to each of six animals. The animals were immobilized in a special holder during the twenty-four exposure period. Upon removal of the patches the resulting reactions were evaluated on the basis weighted scores. Evaluations were again made after seventy-two hours. The final score represents an average of the twenty-four and seventy-two hour readings.

METHOD OF POINT SCORING

FOR

EVALUATION OF SKIN REACTIONS

| A. | Erythema and Eschar Formation | 1 |
|-------------|---|-------------|
| | Very slight erythema (barely perceptible) | 1 2 |
| | Well defined erythema | |
| | Moderate to severe erythema | 3 |
| | (injuries in depth) | A |
| | /mjwies in depth/ | 4 |
| - | Total possible erythema score | 4 |
| в. | Edema Formation | |
| | Very slight edema (barely perceptible) | 1 |
| | Slight edema (edges of area well defined by definite raising) | 2 |
| | Moderate edema (area raised approximately 1 mm.) | 3 |
| | Severe edema (raised more than 1 mm. and extending beyond | |
| | area of exposure) | 4 |
| | Total possible edema score | 4 |
| | Total possible score for primary irritation | - 8 |
| | or sensitization | 8 |
| | | |
| | | |
| | | |
| | | |

Primary Irritation Index

Sensitization

| 2 or lessmild irritant | 2 or lessmild sensitizer |
|---------------------------|-----------------------------|
| 2 - 5moderate irritant | 2 - 5moderate sensitizer |
| 6 or abovesevere irritant | 6 or abovesevere sensitizer |

SCORE SHEETS

Varisoft 475 Varisoft 475 (5% free amine) Varisoft 475 (13.5 wt. % solids) Varisoft 475 (13.5 wt. % solids-5% free amine)

risoft 475

ize Woodard and Calvery

| RABBI | T SKIN | | | |
|---------|---------|---------|------------------|--|
| NTACT | ABR | ADED | COMBINET AVERAGE | |
| 72 HRS. | 24 HRS. | 72 HRS. | | |
| 0/0 | 1/0 | 0/0 | | |
| 0/0 | 1/0 | 0/0 | | |
| 0/0 | 1/0 | 0/0 | 0.92 | |
| 0/0 | 1/0 | 0/0 | | |
| 0/0 | 1/0 | 0/0 | | |
| 0/0 | 2/0 | 0/0 | | |
| | | | | |
| | | | | |
| | | | | |
| 0.67 | | 1.17 | | |

of Compound 0.92

Product Tested

Varisoft 475 (5% Free Amine)

Test Method

Draize Woodard and Calvery

| ANIMAL | | | | | | |
|---------|-----|---------|---------|---------|---------|---------------------|
| | | INTACT | | ABRADED | | COMBINED AVERAGE |
| NO. | SEX | 24 HRS. | 72 HRS. | 24 HRS. | 72 HRS. | |
| 1 | М | 1/0 | 0/0 | 2/1 | 1/0 | |
| 2 | F | 1/0 | 0/0 | 2/2 | 1/0 | |
| 3 | F | 0/0 | 0/0 | 1/1 | 0/0 | 2.55 |
| 4 | M | 0/0 | 0/0 | 2/2 | 1/0 | |
| 5 | M | 1/0 | 0/0 | 1/1 | 0/0 | #* |
| 6 | F | 0/0 | 0/0 | 2/2 | 1/0 | V 40" |
| | | | | | | |
| | | | | | | , |
| | | | | | | |
| AVERAGE | | 0.67 | | 3.83 | | |

Primary Irritation Index of Compound 2.55 Erythema/Edema

oft 475 % wt. solids)

Woodard and Calvery

| RABBI | | | | |
|---------|---------|---------------------|------|--|
| VTACT | ABR | COMBINED AVERAGE | | |
| 72 HRS. | 24 HRS. | 72 HRS. | | |
| 0/0 | 1/0 | 0/0 | | |
| 0/0 | 1/0 | 0/0 | | |
| 0/0 | 1/0 | 0/0 | 0.75 | |
| 0/0 | 1/0 | 0/0 | | |
| 0/0 | 1/0 | 0/0 | | |
| 0/0 | 1/0 | 0/0 | | |
| | | | | |
| | | | | |
| | | | | |
| | | | | |
| 0.5 | 1.0 | | · | |

Compound 0.75

Product Tested

Varisoft 475

(13.5 wt. % solids - 5% free amine)

Test Method

Draize Woodard and Calvery

| ANIMAL | | | | | | |
|---------|-----|---------|---------|---------|---------|---------------------|
| | | INTACT | | ABRADED | | COMBINED AVERAGE |
| NO. | SEX | 24 HRS. | 72 HRS. | 24 HRS. | 72 HRS. | |
| 1 | М | 1/0 | 0/0 | 1/1 | 0/0 | |
| 2 | F | 1/0 | 0/0 | 2/1 | 1/0 | |
| 3 | F | 1/0 | 0/0 | 2/2 | 0/0 | - |
| 4 | M | 1/0 | 0/0 | 2/1 | 0/0 | 1.92 |
| 5 | M | 0/0 | 0/0 | 1/1 | 0/0 | |
| 6 | F | 1/0 | 1/0 | 1/1 | 0/0 | |
| | | | | | | |
| | | | | | | |
| | | - | | | | |
| | | | | | | |
| AVERAGE | | 1.0 | | 2.83 | | |

Primary Irritation Index of Compound 1.9

Erythema/Edema

ACUTE ORAL LD50 TOXICITY STUDY

Varisoft 475 (13.5 wt. % solids)
Varisoft 475 (13.5 wt. % solids - 5% free amine)

METHOD - ACUTE ORAL TOXICITY

A group of approximately 30 albino male and female rats, fasted for twenty-four hours were employed to establish an LD_{50} range for each product under test.

Young adult rats which had not been used for previous test purposes were assigned to various dose levels at random. Both sexes were equally distributed.

The product under test was placed in a glass syringe and introduced through the esophagus into the stomach with a stainless steel catheter.

Animals on the same dosage level were then placed in a common cage with free access to food and water. The animals were observed daily for a two week period. No postmortem, or histopathology examinations were performed in this particular study.

SCORE SHEETS

Varisoft 475 (13.5 wt.% solids)
Varisoft 475 (13.5 wt.% solids - 5% Free Amine)

ACUTE ORAL TOXICITY ASSAY

Varisoft 475 (13.5 wt. % Solids) EXFERIMENTAL DATA

Dosages 0.5 cc./Kg. - 16.0 cc./Kg.

Animals Fasted male & female albino rats

Concentration Undiluted (as received)

Weights 200-300 grams

| Group | No. | Dose | Dose Number and | | | | and | Day | of D | eatha | | | - | | Te | rtel | | |
|-------------|--------|----------------|-----------------|---|---|---|-----|-----|------|-------|---|----|----|----|----|------|-----|----|
| No. Animale | Animab | Level | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 3 ° | D* |
| ı | 5 | 0.5% (Ke. | | | | | | | | | | | | | | | 5 | 0 |
| 11 | 5 | 1.0 cc/Ke. | | | | | | | | | | 1 | | | | | 5 | 0 |
| 111 | 5 | 2 . 0 e.c.iKe. | | | | | | | | | | | | | | | 5 | n |
| ١٧ | 5 | 4.0 c.c./Kg. | | | | | | | | | | | | | | | 5 | 0 |
| v | 5 | 8.0 eciKe | | | | | | | | | | | | | | | 5 | 0 |
| ٧١ | 5 | 16.0cciKe | | | | | | | | | | | | | | | 5 | 0 |
| VII | | ccJKg. | | | | | | | | | | | | | | | | |
| VIII | | c.c.iKg. | | | | | | | | | | | | | | | | |
| ŧΧ | | c.e.lKg. | | | | | | | | | | | | | | | | |
| x | | calke. | | | | | | | | | | | | | | | | |

OBSERVATIONS.

Animals dosed at 0.5 cc./Kg. - 2.0 cc./Kg. did not exhibit any effects from the test material.

At the 4.0 cc./Kg. and 8.0 cc./Kg. dosage levels, slightly unkempt coats were noted for approximately 24 hours after forced feeding.

The animals dosed at 16.0 cc./Kg. exhibited slightly unkempt coats after dosing. Normalcy returned within 2-3 days.

Equally non-toxic to males & females.

D. = Over 16.0 cc./Kg.

D_{ec} = Over 16.0 cc./Kg. (95% Confidence Limits = Not Established)

 $LD_{\infty} = Over 16.0 cc./Kg.$

* D - Deaths

* 8 - Survivale

Bio-Toxicology Laboratories • Toxicity and Applied Research Studies - Animal and Human

ACUTE ORAL TOXICITY ASSAY

Varisoft 475 (13.5 wt. % solids - 5% free amine) EXPERIMENTAL DATA

Doeages 0.5 cc./Kg. - 16.0 cc./Kg. Concentration Undiluted (as received)

Animals Fasted male & female albino rats

Weights 200-300 grams

| Group No. | No. | Dose | Number and Day of Deaths | | | | | | | | | Total | | | | | | |
|-----------|---------|--------------|--------------------------|---|---|---|---|---|---|---|---|-------|----|----|----|----|-----|----|
| No. | Animale | Level | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | s * | D. |
| ı | 5 | 0.5 denke | | | | | | | | | | | | | | | 5 | 0 |
| 11 | 5 | 1.0 c.c.tKs. | | | | | | | | | | | | | | | 5 | 0 |
| 111 | 5 | 2.0 c.c.iKz. | | | | | | | | | | | | | | | 5 | 0 |
| IV | 5 | 4.0 e.e.IKE | | | | | | | | | | | | | | | 5 | 0 |
| v | 5 | 8.0 cc.Ke | | | | | | | | | | | | | | | 5 | 0 |
| VI | | 16.0ce.1Ke | | | | | | | | | | | | | | | 5 | 0 |
| VII | | دديلاء. | | | | | | | | | | | | | | | | |
| VIII | | c.e.iKe. | | | | | | | | | | | | | | | | |
| ıx | | c.c.jKe | | | | | | | | | | | | | | | | |
| x | | cciKs. | | | | | | | | | | | | | Γ | | | |

OBSERVATIONS.

Animals dosed at 0.5 cc./Kg. - 2.0 cc./Kg. did not exhibit any effects from the test material.

At the 4.0 cc./Kg. and 8.0 cc./Kg. dosage levels, slightly unkempt coats were noted for approximately 24 hours after forced feeding.

The animals dosed at 16.0 cc./Kg. exhibited slightly unkempt coats after dosing. Normalcy returned within 2-3 days.

Equally non-toxic to males & females.

iD. - Over 16.0 cc./Kg.

Over 16.0 cc./Kg. (95% Confidence Limits = Not Established)

 $u_{\infty} = Over 16.0 cc./Kg.$

D = Deaths

* 8 — Serviyeb

Bio-Toxicology Laboratories • Toxicity and Applied Research Studies - Animal and Human

SUMMARY & CONCLUSIONS

Varisoft 475
Varisoft 475 (5% free amine)
Varisoft 475 (13.5 wt. % solids)
Varisoft 475 (13.5 wt. % solids - 5% free amine)

| ۴ | & CONCLUSIONS |
|----|---------------|
| ٨_ | .TY DATA |

X. .TY DATA .E Varisoft 475

e Individual Score Sheets
Detailed Information)

STUDIES PERFORMED

DRAIZE EYE IRRITATION

X PRIMARY IRRITATION
ACUTE ORAL TOXICITY

| CE EXE IN | RITATION S | | albino rabbits . | | | | | | | |
|-----------|------------|--------|------------------|-------|--------|-------|--|--|--|--|
| <u> </u> | eyes un | washed | eyes w | ashed | eyes w | ashed | | | | |
| | Total | Mean | Total | Mean | Total | Mean | | | | |
| CTURE | Points | Value | Points | Value | Points | Value | | | | |
| | | | | | | | | | | |
| ea | | | | | | | | | | |
| | | † | | | | | | | | |
| | | | | | | | | | | |
| | | | | | | | | | | |
| nctivae | | | | | | | | | | |

equires labeling under the Federal Hazardous Substances Act.

loes not require labeling under the Federal Hazardous Substances Act.

| IRRITATION STUI | y - F.H.S.L.A. Procedure | 6 | albino rabbits |
|-------------------------|------------------------------|---|----------------|
| imary Irritation Index: | 0.92 (mild primary irritant) | | |

| | RITATION STUDY - D. | | | oino rabbits |
|-----------|--------------------------------|-----------------|-------------------|--------------|
| imary Ir | ritation Index: 0.8 | (mild primary i | rritant) | |
| | | Ratio r | egarding six rabb | oits |
| | Evaluation of | | bservation time | |
| Site | Skin Reaction | 4 hrs. | 24 hrs. | 48 hrs. |
| rt ded | Non-Corrosive Non-Corrosive | 6:6 6:6 | 6:6 6:6 | 6:6 6:6 |

| | AL TOXICITY parenteral dose) | Acute Oral LD ₅₀ Study - 30 albino rats F.H.S.L.A. Procedure - 10 albino rats |
|------------|------------------------------|--|
| ute O | ral LD50 Study: | Federal Hazardous Substances Act Procedure: |
| <u>}50</u> | 95% Confidence Limits | Dosage: 5.0 c.c. or 5.0 gms./Kg. Deaths: |

Requires labeling under the Federal Hazardous Substances Act.

Does not require labeling under the Federal Hazardous Substances Act.

SUMMARY & CONCLUSIONS OF TOXICITY DATA SAMPLE Varisoft 475

(5% Free Amine) (See Individual Score Sheets for Detailed Information)

STUDIES PERFORMED DRAIZE EYE IRRITATION X PRIMARY IRRITATION

ACUTE ORAL TOXICITY

| DRAIZE EYE IF | RITATION S | STUDY | albino rabbits | | | | | | |
|---------------|-----------------|---------------|-----------------|---------------|-----------------|---------------|--|--|--|
| Ĺ | eyes ur | washed | eyes w | ashed | eyes washed | | | | |
| STRUCTURE | Total Points | Mean Value | Total Points | Mean Value | Total Points | Mean Value | | | |
| Cornea | | | | | | | | | |
| Iris | | | | | | | | | |
| Conjunctivae | | | | | | | | | |

Requires labeling under the Federal Hazardous Substances Act. Does not require labeling under the Federal Hazardous Substances Act.

| PRIMARY IRRITATION STUDY | - F.H.S.L.A. Procedure | 6 albino rabbits |
|---------------------------|----------------------------------|------------------|
| Primary Irritation Index: | 2.25 (moderate primary irritant) | |

| | RITATION STUDY - D.C | O.T. Procedure | 6 al | bino rabbits |
|------------|-----------------------------|-----------------|-------------------------------------|----------------|
| Primary Ir | ritation Index: 1.7 | (mild primary i | | |
| Test Site | Evaluation of | Ratio r O | egarding six rab bservation time | |
| Intact | Skin Reaction Non-Corrosive | 4 hrs. 6:6 | 24 hrs. 6:6 | 48 hrs. 6:6 |
| Abraded | Non-Corrosive | 6:6 | 6:6 | 6:6 |

| ACUTE ORAL TOXICITY (single parenteral dose) | Acute Oral LD ₅₀ Study - 30 albino rats F.H.S.L.A. Procedure - 10 albino rats |
|---|---|
| Acute Oral LD50 Study: | Federal Hazardous Substances Act Procedure: |
| LD ₅₀ - 95% Confidence <u>Limits</u> | Dosage: 5.0 c.c. or 5.0 gms./Kg. Deaths: |
| Requires labeling under the Fed Does not require labeling unde | deral Hazardous Substances Act. r the Federal Hazardous Substances Act. |

SUMMARY & CONCLUSIONS
OF TOXICITY DATA
SAMPLE Varisoft 475

(13.5 wt. % solids) (See Individual Score Sheets for Detailed Information) STUDIES PERFORMED

- X DRAIZE EYE IRRITATION
- X PRIMARY IRRITATION
- X ACUTE ORAL TOXICITY

| DRAIZE EYE I | RRITATION S | TUDY | 6 | albino ra | bbits | |
|--------------|-----------------|---------------|-----------------|---------------|-----------------|---------------|
| | 6 eyes unwashed | | eyes w | ashed | eyes w | ashed |
| STRUCTURE | Total Points | Mean Value | Total Points | Mean Value | Total Points | Mean Value |
| Cornea | 0 | 0.0 | | | | |
| Iris | 0 | 0.0 | | | | |
| Conjunctivae | 16 | 2.7 | | | | |

Requires labeling under the Federal Hazardous Substances Act.

X Does not require labeling under the Federal Hazardous Substances Act.

| PRIMARY IRRITATION STUDY | - F.H.S.L.A. Procedure | 6 | albino rabbits |
|---------------------------|------------------------------|---|----------------|
| Primary Irritation Index: | 0.75 (mild primary irritant) | | |

| PRIMARY IRR | ITATION STUDY - D.O | .T. Procedure | 6 al | bino rabbits |
|-------------|---------------------|---------------|-------------------|--------------|
| Primary Irr | itation Index: 0.6 | (mild primary | | |
| | | | regarding six rab | bits |
| | Evaluation of | 0 | bservation time | |
| Test Site | Skin Reaction | 4 hrs. | 24 hrs. | 48 hrs. |
| Intact | Non-Corrosive | 6:6 | 6.6 | ÷ 6:6 |
| Abraded | Non-Corrosive | 6:6 | 6:6 6:6 | 6:6 |

| ACUTE ORAL TOXICITY X (single parenteral dose) | Acute Oral LD ₅₀ Study - 30 albino rats F.H.S.L.A. Procedure - 10 albino rats |
|---|---|
| Acute Oral LD50 Study: | Federal Hazardous Substances Act Procedure: |
| Over 16.0 cc./Kg. Not Established Requires labeling under the Federal | Dosage: 5.0 c.c. or 5.0 gms./Kg. Deaths: |
| wedness reporting ander are redere | al Hazardous Substances Act. Le Federal Hazardous Substances Act. |

SUMMARY & CONCLUSIONS
OF TOXICITY DATA
SAMPLE Varisoft 475

(13.5 wt. % solids - 5% free amine)

(See Individual Score Sheets for Detailed Information)

STUDIES PERFORMED

- X DRAIZE EYE IRRITATION
- X PRIMARY IRRITATION
- X ACUTE ORAL TOXICITY

| DRAIZE EYE I | 6 eyes ur | | | albino ra | | |
|--------------|-----------------|---------------|---------------------------------------|------------------------|--------------|------------------------|
| STRUCTURE | Total Points | Mean Value | eyes w Total Points | asned Mean Value | Total Points | ashed Mean Value |
| Cornea | 0 | 0.0 | | | | 74240 |
| Iris | 0 | 0.0 | | | | |
| Conjunctivae | 18 | 3.0 | · · · · · · · · · · · · · · · · · · · | | | |

Requires labeling under the Federal Hazardous Substances Act.

X Does not require labeling under the Federal Hazardous Substances Act.

| PRIMARY IDDITATION CTITO | | |
|--------------------------|------------------------------|------------------|
| PRIMARY IRRITATION STUDY | - F.H.S.L.A. Procedure | 6 albino rabbits |
| | 1.92 (mild primary irritant) | |
| | 1.32 (IIIII Domary Irritant) | |

| PRIMARY IR | RITATION STUDY - D.C | O.T. Procedure | 6 all | pino rabbits |
|-------------------|--------------------------------|----------------|--|----------------------------|
| Primary I | rritation Index: 1.3 | (mild primary | irritant) | |
| Test Site | Evaluation of Skin Reaction | Ratio | regarding six rablebservation time 24 hrs. | oits |
| Intact Abraded | Non-Corrosive | 6:6 6:6 | 6:6 6:6 | 6: 6 6: 6 |

| (stridte bateritetar dose) | Acute Oral LD ₅₀ Study - 30 albino rats F.H.S.L.A. Procedure - 10 albino rats |
|---|--|
| Acute Oral LD50 Study: LD50 95% Confidence Limits Over 16.0 cc./Kg. Not Established | Federal Hazardous Substances Act Procedure: Dosage: 5.0 c.c. or 5.0 gms./Kg. Deaths: |
| Requires labeling under the Federa X Does not require labeling under th | el Hazardous Substances Act. e Federal Hazardous Substances Act. |

| | | _ | | | |
|-------------|---|---|--|-----------------------|--|
| | | | | | |
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| | | | | ** *** *** ** | |
| | - | - | | | |
| | | | | | |

Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

Attachment 3:

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Report to Northern Petrochemical Company - Eye Irritation Tests with Eleven Samples in Albino Rabbits [IQAC 68122-86-1, 5% dispersion]

REPORT TO

NORTHERN PETROCHEMICAL COMPANY

EYE IRRITATION TESTS WITH ELEVEN SAMPLES IN ALBINO RABBITS

IBT NO. A2182

I. Introduction

At the request of Northern Petrochemical Company, an eye irritation test was conducted with each of eleven samples. The samples were identified as follows:

- 1. Varsulf 142-37, Lot 156-23, 20% Dispersion
- 2. Varsulf 142-37A, 20% Dispersion
- 3. Varifos 156-27, 20% Dispersion
- 4. Varisoft E228/Lot V12-201222, 5% Dispersion
- 5, Varisoft 4757 Lot V34-207309, 5% Dispersion
- 6. Varisoft 3690, Lot V9-209123, 5% Dispersion
- 7. Varisoft SDC, Lot V12-110320, 5% Dispersion
- 8. Varisoft 3262, Ref. 157-8B, 5% Dispersion
- 9. Varisoft 100, Ref. 157-8A, 5% Dispersion
- 10. Adogen 432, Ref. 157-8C, 5% Dispersion
- 11. Varisoft 136-62, 5% Dispersion

II. Sununary

The results of the rabbit eye irritation tests conducted with eleven samples are summarized below.

| | | Res | ults |
|-----------------|--------------|------------------|-----------------------|
| | | Maximum Mean | |
| Test Material | % Dispersion | Irritation Score | Rating |
| | | ,2 | • |
| Varsulf 142-37 | 20 | 21.7/110.0 | Mildly Irritating |
| Varsulf 142-374 | . 20 | 18.3/110.0 | Mildly Irritating |
| Varifos 156-27 | 20 | 41.3/110.0 | Moderately Irritating |
| Varisoft E228 | 5 | 62.0/110.0 | Extremely Irritating |
| Varisoft 475 | 5 | 11.3/110.0 | Minimally Irritating |
| Varisoft 3690 | 5 | 12.0/170.0 | Mildly Irritating |
| Varisoft SDC | 5 | 86.3/110.0 | Extremely Irritating |
| Varisoft 3262 | 5 | 12.6/110.0 | Minimally Irritating |
| Varisoft 100 | 5 | 15.7/110.0 | Mildly Irritating |
| Adogen 432 | 5 | 84.0/110.0 | Extremely Irritating |
| Varisoft 136-62 | 5 | 17.0/110.0 | Mildly Irritating |

Respectfully submitted,

INDUSTRIAL BIO-TEST LABORATORIES, INC.

Report prepared by:

Kenneth Ebbens, B.S.

Assistant Toxicologist

Acute Toxicity

Report approved by:

Carmon Mastri, B.S.

Senior Group Leader

Acute Toxicity

M. L. Keplinger, Ph. D. Manager, Toxicology

III. Investigational Procedure

The same procedure was followed for each test material.

Young albino rabbits of the New Zealand strain were used to evaluate the eye irritating properties of the test material. The test method was patterned after that of Draize et al.*

The test material was instilled into the conjunctival sac of the right eye of each rabbit according to the treatment procedure presented in Table I. The left eye of each animal served as a control.

At each scoring interval the cornea, iris, and palpebral conjunctiva were examined and graded for irritation and injury according to a standard scoring system. The maximum possible score at any one examination and scoring period is 110 points, which indicates maximal irritation and damage to all three ocular tissues. Zero score indicates no irritation. The scoring system is presented in Table II. In this scoring system, special emphasis is placed upon irritation or damage to the cornea, while less emphasis is placed upon damage to the iris and conjunctiva.

After the completion of the test, the scores were analyzed, and a descriptive eye irritation rating was assigned to the test material.

The criteria used for assignment of the descriptive rating are the frequency, the extent, and the persistence of irritation or damage which occur to the three ocular tissues.

^{*} Draize, John II., Woodard, Geoffrey, and Calvery, Herbert O., "Methods for the Study of Irritation and Toxicity of Substances Applied Topically to the Skin and Mucous Membranes," J. Pharm. & Exp. Ther. 82, 377 (1944).

TABLE I

Eye Irritation Tests - Albino Rabbits

Treatment Procedure

| | • | | | | | |
|---------------------------------|----------------------|--------------|---------------------------|--------------------------|----------------------------------|---|
| | Number of Animals | Form | Quantity of Test Material | Contact Period (seconds) | Volume of Wash (tap water) | Scoring Intervals |
| Test Material | Evaluated | Administered | | | | |
| Varsulf 142-37, | က | Undiluted | 0. l ml | Unlimited | None | One minute, one, 24 and 72 hours, and 7 days |
| 20,7 Varsulf 142-37A, 20% | ٣ | Undiluted | 0.1 ml | Unlimited | None | One minute, one, and 72 hours, and 7 days |
| Varifos 156-27, 20% | ٣ | Undiluted | 0. 1 ml | Unlimited | None | One minute, one, 24 and 72 hours, and 7 and 14 days |
| Varisoft E228, | e | Undiluted | 0.1 ml | Unlimited | None | One, 24 and 72 hours, and 7 and 14 days |
| 5% Varisoft 475, 5% | m | Undiluted | 0.1 ml | Unlimited | None . | One minute, one, 24 and . 72 hours, and 7 days |
| Varisoft 3690, 5% | ĸ | Undiluted | 0.1 ml | Unlimited | None . | One minute, one, 24 and 72 hours, and 7 days |
| Varisoft SDC, 5% | en . | Undiluted | 0.1 ml | Unlimited | None | One, 24 and 72 hours, and 7 and 14 days |
| Varisoft 3262, 5% | m· | Undiluted | 0.1 ml | Unlimited | None | One, 24 and 72 hours, and 7 days |

TABLE I (continued)

Eye Irritation Tests - Albino Rabbits

Treatment Procedure

| 5% 3 Undiluted 0.1 ml Unlimited None 5% 3 Undiluted 0.1 ml Unlimited None -62, 5% 3 Undiluted 0.1 ml Unlimited None | Test Material | Number of Animals Evaluated | Form Administered | Quantity of Contact Volume of Test Material Period Wash Administered (seconds) (tap water) | Contact Period (seconds) | Volume of Wash (tap water) | Scoring Intervals |
|---|---------------------|-----------------------------------|----------------------|--|--------------------------------|----------------------------|---|
| 3 Undiluted 0.1 ml Unlimited None, 5% 3 Undiluted 0.1 ml Unlimited None | Varisoft 100, 5% | 3 | Undiluted | | Unlimited | Non e | One minute, one, 24 and 7 days |
| 3 Undiluted 0.1 ml Unlimited None | Adogen 432, 5% | ٣ | Undiluted | 0.1 ml | Unlimited | None | One minute, one, 24 and 72 hours, and 7 |
| | Varisoft 136-62, 5% | m | Undiluted | 0.1 ml | Unlimited | None . | One, 24 and 72 hours, and,7 days |

TABLE II

Eye Irritation Tests - Albino Rabbits

Scale of Weighted Scores for Grading the Severity of Ocular Lesions

| | • | • |
|---------|---|---------|
| Ocular | | |
| Tissues | Description. | Grading |
| Cornea | Opacity (A) | |
| | Opacity - Degree of density (area which is | |
| | dense is taken for reading). | |
| | Scattered or diffuse area, details of iris | |
| | clearly visible. | 1 |
| | Easily discernible translucent areas, details | |
| | of iris slightly obscured. | 2 |
| | Opalescent areas, no details of iris visible, | |
| | size of pupil barely discernible. | 3 |
| | Opaque, iris invisible. | 4 |
| | Area of Cornea Involved (B) | |
| | One quarter (or less) but not zero. | 1 |
| | Greater than one-quarter but less than one- | |
| • | half, | 2 |
| | Greater than one-half but less than three- | |
| • | quarters. | - 3 |
| | Greater than three-quarters, up to whole | |
| | area. | 4 |
| | Score equals A x B x 5 Total maximum = 80 | |
| Iris | Values (A) | |
| | Folds above normal, congestion, swelling, | |
| | circumcorneal injection (any or all of these | |
| - | or combination of any thereof), iris still | |
| | reacting to light (sluggish reaction is | |
| | positive). | 1 |
| | No reaction to light, hemorrhage, gross | |
| | destruction (any or all of these). | 2 |
| | Score equals A x 5 Total maximum = 10 | |
| | | |

TABLE II continued

Eye Irritation Tests - Albino Rabbits

Scale of Weighted Scores for Grading the Severity of Ocular Lesions

| Ocular Tissues | Description | Grading |
|-------------------|--|---------|
| Conjunctiva | Redness (A) | • |
| Conjunctiva | Redness (refers to palpebral conjunctiva only). | |
| | Vessels definitely injected above normal. | 1 |
| | More diffuse, deeper crimson red, individual | |
| | vessels not easily discernible. | 2 |
| | Diffuse beefy red. | 3 |
| | Chemosis (B) | |
| | Any swelling above normal (includes nictitating | , |
| | membrane). | 1 |
| | Obvious swelling with partial eversion of the lids | . 2 |
| | Swelling with lids about half-closed. | - |
| | Swelling with lids about half-closed to completely closed. | 4 |
| | Discharge (C) | • |
| | Any amount different from normal (does not in- | |
| | clude small amount observed in inner canthus | 1 |
| | of normal animals). | • |
| | . Discharge with moistening of the lids and hairs | 2 |
| | just adjacent to the lids. | , 5 |
| | Discharge with moistening of the lids and hairs | 3 |
| | and considerable area around eye. | • |
| | Score $(A + B + C) \times 2$ Total maximum = 20 | |

Note: The maximum total score is the sum of all scores obtained for the cornea, iris, and conjunctiva.

The rating is arrived at by selecting the maximum mean irritation score at one, 24 or 72 hours after instillation. If the rate of dissipation of injury does not meet the requirements defined for the descriptive rating appropriate for a particular numerical score, the descriptive rating is raised by one or more levels. The rating system is presented in Table III.

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TABLE III

Eye Irritation Tests - Albino Rabbits

Classification of Test Materials
Based on Eye Irritation Properties

| Rating | Range | Definition |
|----------------------------|--------------|---|
| Non-Irritating | 0.0 - 0.5 | To maintain this rating, all scores at the 24-hour reading must be zero; otherwise, increase rating one level. |
| Practically Non-Irritating | > 0.5 - 2.5 | To maintain this rating, all scores at the 24-hour reading must be zero; otherwise, increase rating one level. |
| Minimally Irritating | > 2.5 - 15.0 | To maintain this rating, all scores at the 72-hour reading must be zero; otherwise, increase rating one level. |
| Mildly Irritating | >15.0 - 25.0 | To maintain this rating, all scores at the 7-day reading must be zero; otherwise, increase rating one level. |
| Moderately Irritating . | >25.0 - 50.0 | To maintain this rating, scores at 7 days must be ≤ 10 for 60% or more of the animals. Also, mean 7-day score must be ≤ 20 . If 7-day mean score is ≤ 20 but $< 60\%$ of animals show scores < 10 , then no animal among those showing scores > 10 can exceed a score of 30 if rating is to be maintained; otherwise, raise rating one level. |

TABLE III continued

Eye Irritation Tests - Albino Rabbits

Classification of Test Materials
Based on Eye Irritation Properties

| Rating | | Range | Definition |
|------------------------|---|---------------|--|
| Severely Irritating | • | >50.0 - 80.0 | To maintain this rating, scores at 7 days must be ≤ 30 for 60% or more of the animals. Also, mean 7-day score must be ≤ 40 . If 7-day mean score is ≤ 40 but $<60\%$ of the animals show scores ≤ 30 , then no animal among those showing scores > 30 can exceed a score of 60 if rating is to be maintained; otherwise, raise rating one level. |
| Extremely Irritating | | >80.0 - 110.0 | |

· Iniustrial BIO-TEST Laboratories, Inc.

IV. Results

The results of the eye irritation tests are presented in Tables

IV - XIV

TABLE VIII

TEST MATERIAL: Varisoft 475

Eye Irritation Test - Albino Rabbits

ults

| | | | | 7.0 | 7.2 | 7 |
|---------------------|--------|------------------------|------------|-------------------|-------|------|
| | Rabbit | ~ | -4 | * 7 | 7 | |
| | Number | Minute | Hour | Hours | Hours | Days |
| ens: | | • | c | 5 (1-1) | 0 | 0 |
| princa (D-A) | - | > | . 0 | . 0 | 0 | 0 |
| 2 | | 8 (7-1-1) | 12 (2-2-2) | 4 (1-1-0) | 0 | 0 |
| enjunctiva (R-S-D) | | 8 | | 6 | 0 | 0 |
| tal | ı | | c | c | 0 | 0 |
| ernea (D-A) | 7 | > | o c | o | 0 | 0 |
| S | | 6 (2-0-1) | 12 (2-2-2) | 4 (1-1-0) | 0 | 0 |
| enjunctiva (R-S-D) | | 9 | 12 | . 4 | 0 | 0 |
| otal | • | • | c | 0 | 0 | 0 |
| ornea (D-A) | m | - | o c | 0 | 0 | 0 |
| S | | 6 (2-0-1) | 10 (2-1-2) | 4 (1-1-0) | 0 | 0 . |
| onjunctiva (R-S-D) | | 9 | 10 | 4 | 0 | |
| otal | | • | | | | |
| verages | | ٠. ٥ | 0 | 1.7 | 0.0 | 0.0 |
| cornea | | | 0.0 | 0.0 | 0.0 | 0.0 |
| ıis | | - ÷ | 11.3 | 4.0 | 0.0 | 0.0 |
| Conjunctiva | | 6.7 | | 5.7 | 0.0 | 0.0 |
| otal | | der Ser | | | | |
| | Ir | Iris: | Con | Conjunctiva: | | |
| orneat | 14 | Iris Score = Value x 5 | R = | Redness | | |
| = Density | Σ. | Maximum Score = 1 | "S | Swelling | | |
| A street | | | " Q | Discharge | | |
| orneal Score = DxAA | , | * | روي | innetival Score = | | |

-• Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

Attachment 4:

Report from Rosner-Hixson Laboratories, Skin Irritation [IQAC 68122-86-1, 5% dispersion]

ROBNER · HAXSON LABORATORIES

Telephone 7737 South Chicago Avenue/Chicago, Illinois 60619/Area Code 312 REgent 4-0142



Laboratory No. PT72-10

CLIENT:

Northern Petrochemical Company of Des Plaines, Illinois.

SAMPLE:

Varisoft 475, 5% Aqueous Dispersion. 57 s.a.J 1PA

OBJECT:

To determine the skin irritation potential of the sample in accordance with Federal Hazardous Substances Labeling Act Regulations.

EXPERIMENTAL & RESULTS:

The hair was clipped from the abdomen of six male albino rabbits and two areas of the abdomen approximately ten centimaters apart were designated for application of the patches. A one inch square site on the right side was abraded while a similar site on the left remained unabraded.

One-half milliliter of the sample was placed on the skin under a small square of cotton gauze and maintained in contact with the skin under a larger square of polyethylene film and anchored to the skin with strips of adhesive tape. A square of flannel cloth was then taped around the trunk of the animal to further protect the patches from being dislodged.

After 24 hours the vest and patches were removed and the skin examined for signs of irritation (erythems and/or edems). Examination was made again after 72 hours.

Skin irritation scores are presented in Table 2. See Appendix for Evaluation of Skin Reactions in Primary Irritation Test.

The primary irritation score of 0.83 indicates that the sample is not a primary skin irritant.

SUMMARY & CONCLUSION:

Varisoft 475, 5% Aqueous Dispersion, was tested for primary skin irritation in accordance with Federal Hazardous Substances Labeling Act Regulations.

_ Application of sample to intact and abraded skin of rabbits produced a primary irritation score of 0.83. Since minimal score of 5 is required for classification as a primary skin irritant this product is not a primary skin irritant.

On the basis of the test, Varisoft 475, 5% aqueous dispersion, is not a primary skin irritant in accordance with Federal Hazardous Substances Labeling Act Regulations. Consequently, precautionary labeling as a skin irritant is not required.

June 6, 1972

ja



ROSNER-HIXSON LABORATORIES

F. Hixson, Technical Director

-. • . Art No well Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

Attachment 5:

#

WARF Institute Report - Skin Irritation [IQAC 68122-86-1, 5% dispersion]

MADISON, WISCONSIN

Reports are submitted to clients on a confidential basis. No reference to the work, the results or to the Institute in any form of advertising, news release or other public announcement may be made without written authorization from the Institute.

REPORT

Analysis for

Skin Irritation

Description of Sample

Liquid

Date Received

11-5-76

Control Number

Varisoft 475 (5% Active)

Submitted by

Richard M. Egan Ashland Oil, Inc.

Dublin, OH

Claimed Content

Results

Skin Irritation Index: 1.75

Method

Please see attached protocol.

Remarks

Signed

by and for the WARF INSTITUTE, INC.

Date

December 9, 1976

WARF Institute No.

6111267

MADISON, WISCONSIN

PRIMARY SKIN IRRITATION

Client Ashland Oil, Inc.

WARF Institute No. 6111267

Sample Varisoft 475 (5% Active)

Test Animal: Young adult rabbits (approximately 14 weeks of age) of the New Zealand white strain weighing 2.5 to 3.5 kg were procured, maintained individually in screen bottom cages in air conditioned quarters, provided continuous access to commercial laboratory feed and water and held for a conditioning period of at least 7 days.

Method: Conditioned animals were chosen at random, treated and maintained as specified for the conditioning period.

The hair was clipped from the back and flanks of the animal. The test material was applied to two areas on each rabbit, I abraded area, and I intact area, in the amount of 0.5 ml per area in the case of liquids or 0.5 gm per area in the case of solids. The treated areas were covered with a gause patch and taped to maintain the test material in contact with the skin and decrease the rate of evaporation. The animals were ismobilized for a 24 hour period at which time the coverings were removed and the degree of crythems and edems were recorded according to the scale below. A second reading was taken at 72 hours. The average of the 24 and 72 hour readings were used to determine the primary irritation index for the sample.

Concentration of Test Material: as submitted

Results:

| | 24 Hours (1) Abraded Unabraded | | 72 Hours (1) | | |
|--------|--------------------------------|---------|--------------|-----------|--|
| Animal | | | Abraded | Unabraded | |
| Number | Er. Ed. | Br. Ed. | Er. Ed. | Rr. Ed. | |
| 1 | 1 - 1 | 1 - 1 | 1 - 0 | 1 - 0 | |
| 2 | 1 - 1 | 1 - 1 | 1 - 0 | 1 - 0 | |
| 3 | 2 - 1 | 2 - 1 | 1 - 0 | 1 - 0. | |
| 4 | 1 - 1 | 1 - 1 | 1 - 0 | 1 - 0 | |
| 5 | 2 - 1 | 2 - 1 | 1 - 0 | 1 - 0 | |
| 6 | 2 - 1 | 2 - 1 | 1 - 0 | 1 - 0 | |
| Score | 24-hour | 2.50 | 72-hour | 1.00 | |

Primary Skin Irritation Index (2): 1.75

- (1)_ Score equals sum of erythems and edems readings.
- (2) Skin irritation index equals average of 24 and 72 hour scores.

| Erythema and Eschar Formation | Score | Edema Formation | Score |
|-------------------------------|-------|----------------------|-------|
| Slight erytheme | 1 | Slight edema (barely | |
| Defined erythems | 2 | perceptible) | 1 |
| Moderate to severe crythems | 3 | Defined edems (edges | |
| Severe erythema to slight | | definite rising) | 2 |
| eschar formation | 4 | Moderate edema (area | |
| | | raised 1 mm) | 3 |
| | | Severe edema (raised | |
| | | more than 1 mm) | 4 |

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| Attachment 2: Toxicity Studies for Ashland Oil Company [IQAC 68122-86-1, misc. formulations] |
| Attachment 3: Report to Northern Petrochemical Company - Eye Irritation Tests with Eleven Samples in Albino Rabbits [IQAC 68122-86-1, 5% dispersion] |
| Attachment 4: Report from Rosner-Hixson Laboratories, Skin Irritation [IQAC 68122-86-1, 5% dispersion] |
| Attachment 5: WARF Institute Report - Skin Irritation [IQAC 68122-86-1, 5% dispersion] |
| Attachment 6: Dermal Sensitization Study in Guinea Pigs - Raltech Reports Nos. 871605, 871606 & 871607 [IQAC 68122-86-1] |
| Attachment 7: Laboratory Report - Biodegradability [IQAC 68122-86-1] |
| Attachment 8: WARF Institute Reports 8040871 & 8040872 - Skin Irritation, Eye Irritation, Acute Oral Toxicity [PEQ 68410-69-5] |
| Attachment 9: WARF Institute Reports 8040875 & 8040876 - Skin Irritation, Eye Irritation, Acute Oral Toxicity [PEQ 68410-69-5, 5% dispersion] |
| Attachment 10: Toxicity Studies for Ashland Oil Company [PEQ 68410-69-5, 4% and 8% dispersions] |

Continued

CSMA: QUATSREP.FUP

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- Attachment 11: Report to Ashland Chemical Company Acute Toxicity Studies with Varisoft 222 [PEQ 68410-69-5, 4% dispersion]
- Attachment 12: Rosner-Hixson Laboratories Report Acute LD50 [PEQ 68410-69-5, 18% dispersion]
- Attachment 13: WARF Institute Report 7117554 Primary Eye Irritation [PEQ 68410-69-5]
- Attachment 14: Rosner-Hixson Laboratories Report Eye Irritation [PEQ 68410-69-5, 15% dispersion]
- Attachment 15: Rosner-Hixson laboratories Report Skin Irritation [PEQ 68410-69-5, 4% dispersion]
- Attachment 16: Report to Northern Petrochemical Company Primary Skin Irritation of Eight Samples of Shampoo in Albino Rabbits [PEQ 68410-69-5, Full strength and 4% dispersion]
- Attachment 17: Bio-Toxicology Laboratories Report DOT and FSHA Skin Irritation [PEQ 68410-69-5]
- Attachment 18: Report to Ashland Chemical Company Skin Sensitization Test with Varisoft 222 in Albino Guinea Pigs [PEQ 68410-69-5]
- Attachment 19: Delayed Contact Hypersensitivity Study in Guinea Pigs [PEQ 68410-69-5]
- Attachment 20: Raltech Reports Nos. 816078, 816079, 856938, 856939, 856940, 877521, & 877522 Skin Sensitization [PEQ 68410-69-5]
- Attachment 21: Biodegradability, Varisoft 222 [PEQ 68410-69-5]

CSMA: QUATSREP.FUP

CERTIFICATION OF EXPERT REPORT

The report titled:

Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

has been prepared by the undersigned who certifies that any conclusions drawn in this report are based on a reasonable degree of scientific certainty and the training and experience of the undersigned.

John A. Todhunter, Ph.D.

Fellow, American Institute of Chemists Diplomate, American Board of Toxicology

G. Toolle

7-29-93

CSMA: QUATSREP.FUP

Date

BACKGROUND

History and Nature of Present Report

In response to the 22nd Report of the TSCA Interagency Testing Committee ("ITC"), members of the Fabric Softener QUATS Steering Committee ("The Committee"), through the auspices of the Chemical Specialties Manufacturers Association, submitted a large number of studies and reports to U.S. EPA.

In response to these submissions, the ITC, via a letter dated February 22, 1993 from John D. Walker, Exectuive Director, to Jim T. Hill, of CSMA, requested clarification of the relationships among various of the QUATS covered in the aforesaid submissions, justifications for proposing some QUATS as analogs of other QUATS, and various, miscellaneous other points of information.

The Committee engaged its outside consultant, Dr. John A. Todhunter of SRS International Corporation, to review the letter and provide the additional information and/or points of clarification which were requested.

The present report is that prepared by SRS International at the request of the Fabric Softener QUATS Steering Committee.

Scientific Background

The present report deals, in large part, with justification for drawing toxicological analogies between various of the QUATS which are used in fabric softeners.

this regard, it must be noted that most of the toxicoand ecological effects potential of these compounds driven by rather non-specific physico-chemical effects as opposed to compound specific biological interactions. For example, the skin or eye irritancy of these compounds is generally similar and is not very sensitive to whether the test substance is EEQ*, These effects are produced by defatting IQAC or a PEQ compound. the skin or by a similar defatting of and solubilization membrane components in the eye and such effects are a physicochemical effect which is not highly sensitive to differences structure, so long as any changes in the structure does abolish the defatting effect. In contrast to such non-specific effects, these compounds do not appear to have any significant

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^{*} EEQ is not now, nor has it for many years (if ever) been produced for commercial use in fabric softeners. As a result, there are no studies on EEQ. PEQ is, in any case, an excellent analog. EEG is homologous to the PEQ series and is defined as a PEQ with less than an average of 1.5 ethoxy units in the polyethoxy chain.

ability to bind to specific biological receptors (membrane bound or intracellular) and are at best poorly absorbed from the oral or dermal routes of exposure. Thus, they have little if any potential for producing toxic effects on humans, domestic animals, or wildlife (including aquatic organisms) by "classical" mechanisms of toxicity. For these reasons, data on a small number of these compounds will be useful in evaluating other compounds, even if they are in another structural class. Of course, for homologous compounds, the analogy will be quite excellent.

For the above reason, and so as to be as responsive to the ITC's interests for each specific QUAT listed in the 22nd report as possible, data was provided in the previous submissions of the Fabric Softener QUATS Steering Committee on compounds which are analagous to the specific compound for which ITC requested information. In some cases the analog is of the same structural class. In some other cases, the analogs were of a different structural class but, due to the non-structure specific mechanisms for production of the effects of interest, were considered to provide appropriate information as to the toxicity potential of the specific compound of interest to ITC. In a few other cases, if any toxicological effect were possible, it would be produced via interactions with specific functional groups which are common between different structural classes of the quaternary ammonium compounds at issue.

In the detailed responses to the ITC's letter of February 22, 1993 which follow, the appropriate structural information is provided for ITC's reference and ease of comparison. Also, the basis upon which specific analogs were proferred is provided.

CSMA: QUATSREP.FUP

Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated February 22, 1993 from Dr. John D. Walker, Executive Director, TSCA Interagency Testing Committee, to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to Data Submissions from QUATS Steering Committee Members Filed in Response to the 22nd Report of the TSCA Interagency Testing Committee

Attachment 6:

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Dermal Sensitization Study in Guinea Pigs - Raltech Reports Nos. 871605, 871606 & 871607 [IQAC 68122-86-1]



P O Box 7545 • Madison Wisconsin 53707 • 808/241-4471 A Division of Reliston Purine Company

REPORT

MR ROFERT L. FARRISON SHFREW CHEMICAL COMPANY, INC. P.O. F.Y 646 DUFLIN, DH 43017

RT LAB NO. 871605

ENTERED 06/16/81

REFORTER 09/18/81

VARISHFT 475: LOT 1138

PURCHASE OFFIER MUMBER 021-49378

ENCLOSED:

DEFRAL SENSITIZATION STUDY IN GUINEA PIGS

(MODIFIED CLOSED PATCH TECHNIQUE) - METHOD, SUMMARY

RAW DATA ATTACHED

SIGNED:

TARY W. THOMESON, ES

MANAGEP, ACUTE TOXICOLOGY

PY AND FOR RALTECH SCIENTIFIC JERVICES, INC.



PO Box 7545 • Madison, Wisconsin 53707 • 608/241-4471

A Division of Raiston Purina Company

T LAB NUMBER 871605

ARISOFI 475: LOT 1139K

PAGE 2

SKIN SENSITIEATION

OBJECTIVE: TO DETERMINE THE DELAYED CONTACT HYPERSENSITIVITY POTENTIAL OF A TEST MATERIAL IN GUINEA PIGS.

TEST ANIMAL: TWENTY-FOUR ACCLIMATED GUINEA FIGS, WEIGHING FROM 333 TO 426 G WERE USED FOR THIS STUDY. THE ANIMALS WERE DIVIDED INTO TWO GROUPS CONSISTING OF A NAIVE CONTROL GROUP OF FOUR GUINEA PIGS AND A TREATED GROUP OF TWENTY GUINEA FIGS. AN EQUAL NUMBER OF MALE AND FEMALE ANIMALS WERE PLACED IN EACH GROUP. THE ANIMALS WERE IDENTIFIED BY ANIMAL NUMBER AND EAR TAR. THE ANIMAL WERE INDIVIDUALLY HOUSED IN SCREEN-POTTOM CAGES IN TEMPERATURE AND HUMIDITY CONTROLLED ROOMS. ANIMALS WERE PROVIDED CONTINUO ACCESS TO PURINA GUINEA PIG CHOW AND WATER THROUGHOUT THE STUDY PERIOD.

PREPARATION OF TEST MATERIAL: TO PREPARE A 1.0% WEIGHT/VOLUME MIXTURE, 1.0 OF VARISHET 475: ICT 1138K WAS WEIGHED INTO AN ERLENNEYER FLASK. STERILE 0.9% SALINE WAS ADDED TO MAKE A TOTAL VOLUME OF 100 ML. THE MIXTURE WAS THEN STIRRED USING A STIR PLATE AND A MAGNETIC STIR PAR TO A UNIFORM SUSPENSION. THE TEST MATERIAL WAS PREPARED FRESH PRIOR TO EACH APPLICATION.

TREATMENT: THE DAY BEFORE EACH APPLICATION THE HAIR WAS REMOVED FROM THE LEFT SHOULDER OF EACH ANIMAL WITH ELECTRIC CLIPPERS. THE TEST MATERIAL WAS AFFLIED TO ONE ALEA ON EACH ANIMAL BY PLACING 0.4 ML OF THE FRESHLY PREPARED TEST SUBSTANCE ON A MEBRIL PAD (7/8 INCH X 1 INCH) AND PLACING THE PAD ON THE TEST SITE ALONG THE MIDLINE OF THE BACK. THE FATCH WAS COVERED WITH EUBBET DAM AND DECUPED WITH AN OVERWEAP OF ELASTOPLAST TAPE. THE DEESSING REMAINED IN FLACE FOR A PERIOD OF SIX HOURS AT WHICH TIME IT WAS AS YOVED. THE TEST MATERIAL WAS REMOVED BY A GENTLE RINSE WITH WARM WATER BEFORE FETURNING THE ANIMALS TO THEIR CAGES.

THE ANIMALS RECEIVED ONE APPLICATION PER WEEK FOR THREE WEEKS FOR A TOTAL OF THEFE APPLICATIONS.

TWO WEEKS FOLLOWING THE ADMINISTRATION OF THE THIRD SENSITIZING DOSE, A CHALLFYSE DOSE AT A VOLUME OF C.4 ML WAS ADMINISTERED TO THE TEST GROUP IN THE SAME MANNER AS DURING THE SENSITIZING PHASE OF THE STUDY. AT THIS TIME, THE FOUR NAIVE (PREVIOUSLY UNTREATED) CONTROL ANIMALS WERE ALSO THEATED WITH A CHALLFNGE APPLICATION. THE CHALLENGE APPLICATIONS WERE MAD TO A PRESHLY CLIPPED SKIN SITE THAT HAD NOT PEEN PREVIOUSLY TREATED. TWENTY-FOUR HOURS AFTER PRIMARY CHALLENGE, THE ANIMALS WERE DEPILATED WITH NEET CREAM HAIR FEMONER (WHITEHALL LABORATORIES, INC., NEW YORK). THE DEPILATORY WAS APPLIED ON THE TEST SITES AND SURROUNDING AREAS FOR THIRTY MINUTES. THEN THE DIFILATORY WAS THOROUGHLY WASHED OFF WITH WARM WATER, THE ANIMALS DRIED WITH A TOWEL AND RETURNED TO THEIR CAGES.

CBSERVATIONS: THE APPLICATION SITES WERE READ AND SCORED FOR EPYTHEMA AND EDEMA AT 24 AND 48 HOURS FOLLOWING EACH APPLICATION DURING THE SENSITIZING PHASE OF THE STUDY. FEACTIONS TO THE CHALLENGE DOSE WERE READ AND SCORED THO HOURS AFTER DEFILIATION AND 24 HOURS LATER (48 HOUR SCORES). THE ANIMA WERE OBSTRYED FOR GENERAL BEHAVIOR AND APPEARANCE ONCE DAILY DURING THE



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EER 871605

... LOT 113:K

PAGE 3

TIZATION (CONTINUED)
STUDY PERIOD. BODY WEIGHTS WERE TAKEN AT STUDY INITIATION AND AT
LAIERVALS DURING THE STUDY.

T: AT STUDY TERMINATION ALL ANIMALS WERE EUTHANATIZED AND DISCARDED.

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T LAB NUMBER 871605

/PRISPET 475: LOT 1138K

FAGE 4

SKIN SENSITIZATION (CONTINUED)

TEST ANIMAL: GUINEA FIGS

SOURCE: DEAN DAUL, LUNEMBURG, WI

DATE A"IMALS RECEIVED: 7/10/81

DATE TEST STARTED: 7/22/81

DATE TEST COMPLETED: 8/21/81

SUMMARY OF SKIP REACTIONS**

| ANIMAL | ThF | N DITIZIN EF APPLI THEMA | G PHAS CATION EDE | S | Si | CHALLENGI INGLE API | PIICATI | ON |
|--|---|------------------------------------|--|--|---|--|--|--|
| MUNPER 64100368 64100370 64100371 64100372 64100373 64100375 64100376 64100377 | AVF. 0.0 0.0 0.0 0.0 0.0 0.0 0.0 | (HIGH) (0) (0) (0) (0) (0) (0) (0) | A VE . 0 . 0 0 . 0 0 . 0 0 . 0 0 . 0 0 . 0 0 . 0 0 . 0 0 . 0 0 . 0 0 . 0 | (HIGH) (O) (O) (O) (O) (O) (O) (O) (O) (O) | A VE. 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0 | (HIGH) (0) (0) (0) (0) (0) (0) (0) (0) (0) | AVE. 0.0 0.0 0.0 0.0 0.0 0.0 | (O) (O) (O) (O) (O) (O) |
| NAIVE CONTEC 64100393 | ;r | UNTFEAT | red | | 0.3 | (0.5) | - 0-0 | (0) |

0.3 (0.5) 0.0 64100394 (0) UNTREATED 0.0 (0) 0.0 (0) **THE AVERAGE ENTHEMA AND EDEMA VALUE IS THE MEAN SCORE FOR THE SIX OBSE TIONS (SENSITIZING TERATMENT) OR TWO OBSERVATIONS (CHALLENGE? TREATMENT) THE APPLICATION SITE FOR EACH ANIMAL. THE HIGH READING IS THE HIGHEST

SCORE RECORDED FOR THE RESPECTIVE ANIMAL DURING THAT PHASE OF THE STUDY.

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I LAB NUMBER 871605

ARISOFT 475: LOT 1136K

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EKIN SENSITIZATION (CONTINUED)

TEST ANIMAL: GUINEA FIGS

SOURCE: DEAN DAUL, LUYEMBURG, WI

DATE ANIMALS RECEIVED: 7/10/81

DATE TEST STARTED: 7/22/81

DATE TEST CONFLETED: 8/21/81

SUMMARY OF TKIN REACTIONS** (CONT.):

| | S | SENSITIZI | ING PHA | TEST GROUP | · · · · · · · · · · | S !ALLENGE | FHASE | |
|--|--|---|---------|--|---|---|-------|--|
| ANIMAL NUMPER 64100419 64100421 64100422 64100423 64100426 64100430 64100431 64100432 | EFY AVE. 0.0 0.0 0.0 0.0 0.0 0.0 0.0 | FEE APPI THEMA (HIGH) (O) (O) (O) (O) (O) (O) | | (O) (O) (O) (O) (O) (O) (O) (O) (O) (O) | SIN ERY AVE. 0.0 0.3 0.0 0.0 0.3 0.0 0.3 | GLE APPI THEMA (HIGH) (O) (O.5) (O) (C) (O.5) (O) (O.5) (O) | | O) (O) (O) (O) (O) (O) (O) |
| NAIVE CONTROL | | | | | | | | |

| 54100424 64100425 | UNTREATED UNTREATED | | 0.0 | (O) | 0.0 0.0 | (0) |
|------------------------|------------------------|--------------|------------|-----|------------|-------|
| **THE AVERAGE ERYTHEMA | AND EDEMA | VALUE IS THE | MEAN SCORE | FDF | THE CTY | APEE: |

TIONS (STASTITIZING TREATMENT) OR TWO OBSERVATIONS (CHALLENGER TREATMENT) OF THE APPLICATION SITE FOR EACH ANIMAL. THE HIGH READING IS THE HIGHEST PEADING FOR THE RESFECTIVE ANIMAL DURING THAT PHASE (F THE STUDY.

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A Division of Raiston Purina Company

T LAP NUMBER - 871605

HRISTET 475: LOT 1138K

PAGE 6

OKIN BENGITIZATION (CONTINUED)
RESULTS:

GENERAL BEHAVIOR AND AFFEARANCE: ALL OF THE GUINEA PIGS USED IN THIS STUDY AFFEARED NORMAL THEOUGHOUT THE STUDY PERIOD. NORMAL BODY WEIGHT GAINS WER RECONDED FOR ALL ANIMALS DURING THE COURSE OF THE STUDY.

SKIN REPORTIONS TO VARIE CFT 475: LOT 1138K (1.0% W/V AQUEOUS):

ONE MAIE ANIMAL (NO. 64100374) AND THREE FEMALE ANIMALS (NOS. 64100420, 64100426 AND 64100436) REACTED TO THE CHALLENGE APPLICATION WITH A VERY FAINT NONCONFLUENT EFYTHEMA AT THE 24 HOUR OBSERVATION.

ONE MALE ANIMAL (NO. 64100376) IN THE NAIVE CONTROL ALSO RESPONDED WITH A VERY FAINT NONCONFLUENT ERYTHEMA AFTER RECEIVING 0.4 ML OF THE 1.0% W/V

PFCAUSE THE SKIN SEACTION IN THE TREATED ANIMALS DID NOT EXCEED THE MOST SEVERE CONTROL RENCTION, THE RESPONSES WERE NOT SUBSTANTIAL ENOUGH TO BE CONSIDERED POSITIVE FOR SENSITIZATION.

CONCLUSION: DECAUSE NO SENSITIZATION WAS DETECTED IN THIS STUDY, THIS TEST MATERIAL IS NOT CONSIDERED A STRONG SKIN SENSITIZER.

#1 - X

Dermal Sensitization In Guines Pigs - Body Weights

Test Group RT No. 871605 Vehicle 0.9% saline Test Compound Lot 1138 K

NA Positive Control Group NA Vehicle NA

| Dex | | | | _ | | | | | |
|------|---------------|----------------------|---------------|---------------|---------------|---------------|------|-----------------|----------|
| | | | Animal | Number | | | | 1 | |
| 0368 | 6410- 0369 | 6410- 0370 | -0140 1750 | 6410- 0372 | 6410- 0373 | 0410- 0374 | 0375 | Tech- nician | Dat / 98 |
| 420 | 414 | 386 | 1121 | 110 | | | | | - |
| | | | 426 | 401 | 384 | 342 | 394 | وع َ | 7/23 |
| 485 | 473 | 438 | 489 | 471 | 463 | 405 | 490 | NDO | 7/29 |
| 567 | 540 | 500 | <i>55</i> 9 | 558 | 538 | 480 | 590 | | 8/5 |
| 630 | 603 | 576 | 625 | 622 | 607 | 553 | 676 | De | |
| 705 | 668 | 643 | 668 | 685 | 679 | 582 | 730 | ER | 81. |
| | | | | | | | | | -6/1 |

| | | Animal Number | 7 | |
|------|-------------|--------------------------|-------|-------------|
| | 6410- | | | |
| 0376 | 0377 | <u>.</u> | Tech- | Date /98 |
| 386 | 370 | Scale Used: K. Tron 4809 | εR | - |
| 453 | 443 | Scale Used: K-Tron 4809 | י אסס | 7/29 |
| 53% | <i>5</i> 25 | Scale Used: K-Tron 4809 | A 500 | 8/5 |
| 628 | 586 | Scale Used: K-TRON 4809 | SE SE | 8/12 |
| 690 | 642 | Scale Used: K. Tron 4809 | ER | 8/19 |
| | _ | _ Scale Used: | - CIE | 0117 |

Dermal Sensitization in Guinea Pigs - Daily Observations

Sterile

Varisoft 475:

Test Group RT No. 871605 Vehicle 0.9% salingest Compound Lot 1/38 K

NA

Positive Control Group NA Vehicle NA Room No. 2

| | ex é | 3 | | | | • | DOE NO. | | |
|------------|------|------|-----------|---------------|-----|---|---------|------|--------------|
| | | | rinel Num | ber | | | | 7 | |
| 0368 | _ | 0370 | 0371 | 6410- 0372 | | | | | Data 1981 |
| N_ | N | N | N | N | N | N | N | 93 | 7 32 |
| N | N | N | Ν | N | N | N | N | 55 | 7/23 |
| N | l N | N | N | N | N | N | N | JR | 7/24 |
| N | N | N | N | N | N | N | N | 5 | 725 |
| <u> </u> | · N | N. | N | 1/ | N . | N | N | JK | 7/26 |
| N | N | N | <u> </u> | N | N | N | N | IR | 7/27 |
| N | N | N | N | | N | N | N | NO0 | 7/28 |
| | N | N | N | N | N | N | N | 120 | 7129 |
| 2 | N | 12 | · N | <u></u> | N | N | N | m | 7/30 |
| <u>. M</u> | N | N | N | <u> </u> | - 1 | N | - | De | 7/31 |
| 2 | | N | N | N | N | N | N | Cf | 8/1 |
| 2 | ~ | ~ | 2 | 2 | 2 | N | N | del | 8/2 |
| 7 | 0 | 2 | 2 | D D | N | 2 | 2 | du | 8/3 |
| N | N | N | N | | | N | N | | 8/4 |
| N | N | N | N | N | | N | 1 | R | 8/5 |
| N | N | N | N | N | N | N | | 100 | 80 |
| N | N | N | N | N | N | N | N | IP I | 8/7 9/y |

N - No Visible Abnormalities

Dermal Sensitization in Guinea Pigs - Daily Observations

Sterile

Varisoft 475 Test Group RT No. 8711605 Vehicle 0.9% saline Test Compound Lot //38 K NA Positive Control Group NA Vehicle NA Room No. 2 Sex o Animal Number 6410-6410-0376 10377 Technicien Date 1981 N 7/22 ER N 7/23 ER. N 7/24 IK 7/25 7/26 N 1P N N S N 7/29 2 N 7/30 N N 7/3/ と 2 8/2 740 8/3 8/4 clov 8K N 876 100 N Ν 8/7 23

N - No Visible Abnormalities

3/8

NA - Not Applicable

1

Dermal Sensitization in Guinea Pigs - Daily Observations

Sterile

Varisoft 475:

Test Group RT No.871605 Vehicle 0.9% salingest Compound Let 1/38 K

NA Positive Control Group NA Vehicle NA Room No. 2

| | Sex | 3 | | | | | | | |
|----------------------|--------|-----------|-----------|---------------|--------------|---------------|---------------|-----------------|--------------|
| | | 7 | inal Numi | A. | | | | 7 | |
| 6410- 0368 | | 0370 | 0371 | 0410- 0372 | | 6410- 0374 | 0375 | Tech- nicien | Date 1981 |
| N | N | N | N | N | N | N | N | | 8/9 |
| N | N | N | \sim | N | N | N | N | IP 10 | 8/10 |
| N | N | N | N | N | \checkmark | N | N | du | |
| M | N | N | ~ | ٨/ | N | \sim | N | JR DR | 8/11 5/- |
| N | N | N | N | N | N | N | N | EP. | 8/13 |
| N | (1) | N | N | N | N | N | N | | 8/14 |
| <u>N</u> | | - N | N | · N | ٧. | N | N | Ne | 8/15 |
| N | ~ | ->- | | - ~ | N | N | N | Sa | 8/12 |
| N | N | <i>\\</i> | N | N | N | N | | | 117 |
| N | - N | _/_ | ~ | N | -1 | N | N | , - | 8/18 |
| W | N | N | N. | Ņ | N | N | N | ΕS | 8/19 |
| N | N | N | N | N | N | N | | dw 2 | 3/20 |
| | \sim | ~ | N | N | N | N | N | dev 8 | /2/ |
| | | | | | | | | | |
| | | | | | | | | | |
| | | | | | | | | | |
| | | | • | | | | \rightarrow | | |
| | | | | | | | | | |

N - No Visible Abnormalities

Dermal Sensitization in Guines Pies - Daily Observations Varisoft 475 Test Group RT No. 871160 5 Vehicle 0.9% saline Test Compound Lot 1/38 K NA Positive Control Group NA Vehicle NA Room No. 2 Sex 3 Animal Number 6410- 6410-0376 10377 Technicien Date 1981 3/9 da 8/10 8/11 N N 8/13 23 des 8/11 8/15 8/16 N 8/17 8/18 N 5 1: ER N 8/20 de N N 8/21 dev

N - No Visible Abnormalities

| X | DERMAL S Test Group: | RT No. 87 | I STUDY | IN GUINEA S Vehicle <u>o</u> | PIGS Herite 1990 saline | Test Material | Vari: | 1138 1138 |
|----------|----------------------|-----------|---------|------------------------------------|-------------------------------|------------------|---------------------|--------------|
| NA | Positive Control | Group | NA | Vehicle | NA_ | _ Apimal N | 6410 <u>0</u> .0 | ာ- 368 |
| | nimal Received | | | _ | 1 | Date Initi | a ted | Tlas |
| Source | Dean Day | 1 Sez | · _ 3 | | . c a | allenge D | ate | المالع |

| | • | | | * 4 | rec. | i es | |
|------------------------------|---------------------------|-------------------------------------|----------|---------|------------------|------------|--------------|
| Sensi- tizing Dose No. | Dose ⁴ (ml) | Obser- vation Period (Rrs) | Erythema | Zd case | mician | ecorded By | 1981 |
| | 0.4 | RA | RA · | MA | 3 | R | 7/22 |
|] | 1.0% | . 24 48 | 8 | 2 | EP | WP. | 7/23 |
| 2 | 0.4 | MA | NA . | NA | B | an | 7129 |
| a | 1.0% | 24 48 | 9 | S | M | 70 | 7/30 |
| 2 | 0.4 | NA | NA | · | 7 | B | 8/5 |
| 3 | 1.0% | . 24 48 | 00 | 0 | ADO EP | NM | 810 817 |
| Challenge | 0.4 | NA | NA | NA | 50 | ٤٥ | 8 19 |
| Dose | 1.0% | 24 48 | 9 | 0 | 5 <u>2</u> El | 182 | 8/20 8/21 |
| | | NA | NA NA | NA | ., | à' | |
| | | 24 48 | | | | | |

a - Dosage applied by technician indicated
 NA - Not Applicable

| • | DERMAL S | DINCE AND | ATION | STUDY | IN GUIN | A PIGS | | Va =: | ے ۔ |
|-------------|------------------|-----------|-------|-------|---------|------------------------|------------------|------------|------|
| \boxtimes | Test Group: | RT No. | 8716 | 05 | Vehicle | Sterile 0.9% saline | Test Material | <u>Lot</u> | 1138 |
| NA | Positive Control | | | | | | | 641 | 0- |
| Dete Ar | nimal Received | 7/1 | 0 81 | | _ | 1 | Date Initi | a ted | 7/22 |
| Source | Dean Day | 1 | Sex | 7 | | | mallanga D | 474 | alic |

| | | | | | a ect | Sec | |
|------------------------------|---------------------------|-------------------------------------|----------|----------|-----------|------------|------|
| Sensi- tizing Dose No. | Dose ⁴ (ml) | Obser- vation Period (Hrs) | Erythena | Edema | nician | ecorded By | 981 |
| | 0.4 | RA. | RA | KA | B | 3 | 7/02 |
| | 1.0% | 24 48 | 0 | 0 | FP. | MR | 7173 |
| | 0.4 | MA | NA | NA | 1250 | NOW | 7/29 |
| ょ | 1.0.% | 24 48 | 0 | 0 | 200 | 740 Na | 7/30 |
| 2 | 0.4 | MA | NA | · | R | R | 815 |
| 3 | 1.0% | 24 48 | 0 | 0 | NDO ER | NOV SE | 810 |
| Challenge Dose | 0.4 | KA | MA | NA | ED. | ER. | 8/19 |
| Dose | 1.0% | 24 | <u>ာ</u> | 0 | 5.P. | EP. | 8/20 |
| | | - HA | MA | NA | | <u>ئ</u> | |
| | | 24 | | | | | |
| | | 48 | | <u> </u> | | <u> </u> | |

a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN CULTURA BY

| Test Group: | RT No. 871605 | | |
|----------------------|---------------|-------------|--------|
| NA Positive Control | Group NA | _ Vehicle _ | NA Ani |
| Date Animal Received | · | | Date |
| | | | Challe |
| | | | Tech |

| Sensi- tizing Dose No. | Dose ⁴ (ml) | Obser- vation Period (Hrs) | Erythema | Edena | Technician |
|------------------------------|------------------------|-------------------------------------|----------|-------------|------------|
| 1 | 0.4 | RA | RA | NA | R |
| | 1.0% | 24 48 · | 0 | G | ER |
| 2 | 0.4 | NA | NA | NA | NOO |
| 2 | 1.0% | 24 48 | 9 | Q | NDO |
| 3. | 0.4 | NA | NA | · RA | R |
| J. | 1.0% | 24 48 | 00 | 0 | NOV ER |
| Challenge | 0.4 | NA | NA | NA | s Q |
| Dose | 1.0% | 24 48 | | 0 | ςL |
| | | - HA | MA NA | € NA | EL. |
| | | 24 48 | | | |

a - Dosage applied by technician indicated
 NA - Not Applicable

| • | PANTAL S | ENSTITY TIL | N STRBA | IN GUINE | A PIGS | | | |
|--------|------------------|-------------|---------|----------|--------|------------------|---------------------|------|
| X | | | | | | Test Material | Vari L <u>ot</u> | 1138 |
| • | Positive Control | Group | | | | | | |
| | nimal Received | | | - | 1 | Cate Initi | a ted | 7/2. |
| Source | Dean Day | Ser | 3 | | C. | ellenes B | | ماره |

| | • | | | | 2 | L | T |
|------------------------------|------------------------|-------------------------------------|----------|--------|--------------------------|-------------|-------------|
| Sensi- tizing Dose No. | Dose ⁴ (ml) | Obser- vation Period (Hrs) | Erythema | Edens | shnisian | Recorded By | 981 |
| | 0.4 | KA | KA | NA | R | JP | 7/22 |
| | 1.0% | 24 | 0 | 0 | ٤٤ | ME | 7/23 |
| 2 | 0.4 | NA | NA NA | NA | 1000 1000 | NOO | |
| 2 | 1.0% | 24 48 | 0 | 0 | KURO | 10 | 7/30 |
| 3 | 0.4 | NA | NA | . RA | R | R | 7/31 8/5 |
| | 1.0% | · 24 | · () | 0 | 100 | NOO | 86 |
| Challenge Dose | 0.4 | KA | KA | NA. | ER ER | 56 | 8 19 |
| Dose | 1.0% | 24 48 | O | O D | ε β Ε β | ER. | 8/2/ |
| | | -MA | · NA | NA | | ÷' | |
| | | 24 48 | | | | | |

a - Dosage applied by technician indicated NA - Not Applicable

| • | DERMAL | SENSITIZATI | ON STUDY | IN GUINE | PIGS |
|---------|------------------|-------------|----------|-----------|------|
| X | Test Group: | RT No. 8 | | | |
| NA | Positive Control | Group | NA | _ Vehicle | NA |
| Date Ar | nimal Received | 7/10/ | 81 | _ | |

| | | | | , | Tech |
|------------------------------|---------------------------|-------------------------------------|----------|--------------|------------|
| Sensi- tizing Dose No. | Dose ^a (ml) | Obser- vation Period (Rrs) | Erythema | Edena | rechnician |
| , | 0.4 | RA. | NA | NA | |
| ' | 1.0% | 24 | 0 | \bigcirc | - |
| | 1.0 10 | 48 | 0 | 0 | |
| ر ا | 0.4 | KA | RA | NA | N |
| 2 | 1.0.% | 24 | 0 | Q | V |
| | 1.0.70 | 48 | C | 0 | 1 |
| 3 | 0.4 | NA | NA | Na | |
| ・ | 1.0% | 24 | | O | N |
| | | 48 | 0 | 0 | |
| Challenge | 0.4 | NA | NA | - NA | ٤ |
| Dose | 1.0% | 24 | C | O | - |
| | 1.0 /6 | 48 | 0 | 0 | |
| | | - NA | NA ÷ | NA | i |
| | | 24 | | | |
| | • | 48 | _ | | |

a - Dosage applied by technician indicated
 NA - Not Applicable

Source Dean Daul

DERMAL SENSITIZATION STUDY IN GUINEA PIGS
Sterile Test Varisoft 475:

Test Group: RT No. 871605 Vehicle 0.9% soling Material Let 1138 K

WHIONA Positive Control Group NA Vehicle NA Animal No. 0373

Date Animal Received 7/20/81

Source Doop Day 1 Sex 6 Challenge Date 8/19/81

| | | | | | ec. | 200 | |
|------------------------------|---------------------------|-------------------------------------|----------|-------|---------|------------|--------------|
| Sensi- tizing Dose No. | Dose ⁴ (ml) | Obser- vation Period (Hrs) | Erythema | Eduna | micie | scorded by | 1981 |
| 1 | 0.4 | RA | NA | · KA | R | R | 7/2 |
| | 1.0% | 24 48 | 000 | 0 | EP) /_ | JK. | 7/24 |
| 2 | 0.4 | NA | NA | NA | NON | RON | 7/29 |
| | 1.0% | 24 | 8 | 0 | KOO | 790 | 7/30 |
| 3 | 0.4 | MA | NA | · NA | R | R | 815 |
|) | 1.0% | 24 48 | 00 | 0 | NOW | W | 80 |
| Challenge Dose | 0.4 | RA | NA. | NA | 50 | FR | 8/19 |
| Dose | 1.0% | 24 48 | 3 | 0 | 8 D | 50 | 8 70 8/2/ |
| | | KA | NA | NA. | | | <i>₹′</i> |
| [| | 24 | | | | | |
| | | 48 | | | | | |

a - Dosage applied by technician indicated

NA - Not Applicable

Orecording error 7/21/81 ER

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Sterile Test Varisoft

Test Group: RT No. 871605 Vehicle 0.9% Saline Material Lot 1138

6410
NA Positive Control Group NA Vehicle NA Animal No. 0374

Source Dean Daul Sex 6 Challenge Date | B| 19

| | * | | | | er er | 7 | |
|------------------------------|---------------------------|-------------------------------------|----------|-------|-----------|------------|-------------|
| Sensi- tizing Dose No. | Dose ² (ml) | Obser- vation Period (Hrs) | Erythema | Edema | hnisian . | ecorded by | 981 |
| | 0.4 | NA. | RA | KA | R | 7 | 7/22 |
| | 1.0% | 24 48 | 0 | 0 | E. IR | WE | 7/23 |
| 2 | 0.4 | KA | MA | NA | 1200 | NDR | 7/24 |
| a | 1.0.% | 24 48 | 0 | 9 | NO | M | 7/50 |
| 3 | 0.4 | NA | NA | · NA | R | R | 7/3/ 8/5 |
| <u> </u> | 1.0% | 24 48 | | 0 | NOW | LOO | 810 |
| Challenge Dose | 0.4 | NA | NA | NA | 5P. | FR. | 8 7 |
| Dose | 1.0% | 24 48 | 0.5 | 0 | se se | se dev | 8/21 |
| | | · NA | NA | NA | | â' | <u> </u> |
| | | 24 48 | | | ·. | | |

a - Dosage applied by technician indicated

NA - Not Applicable

-

| • | DERMAL S | Ensitiza | TION STUDY | IN GUIN | A PIGS | | | ٥. |
|-------------|------------------|----------|------------|-----------|------------------------|------------------|---------------------|--------------|
| \boxtimes | Test Group: | RI No. | 871605 | Vehicle | Sterile 0.9% saline | Test Material | Vari L <u>ot</u> | 113 <u>8</u> |
| NA | Positive Control | Group _ | NA | _ Vehicle | NA | _ Animal No | 641 | o- 375 |
| Date Ar | imal Received | 7/10/8 | 31 | _ | 1 | Date Initia | ted | العماد |
| Source | Dean Day | 1 | Sex | | | nallenge De | | |

| | • | | | | e c | 6 | L |
|------------------------------|---------------------------|-------------------------------------|----------|-------|-------------|------------|--------------|
| Sensi- tizing Dose No. | Dose ^a (ml) | Obser- vation Period (Rrs) | Erytheme | Edena | haician | ecorded by | 981 |
| | . 0.4 | RA | RA | NA | R | SP | 7/12 |
| | 1.0% | 24 48 | . 0 | 0 | وو. عالا | WZ | |
| 2 | 0.4 | NA | KA | NA | NOO | ran | 7129 |
| 2 | 1.0.% | 24 . 48 | 0 | 8 | 1000 | 100 | 7/30 |
| 2 | 0.4 | NA | NA | · NA | R | R | 815 |
| 3 | 1.0% | 24 48 | 0 0 | D | NON | NTO | |
| Challenge | 0.4 | RA | RA | NA | FD | ER | Bliq |
| Dose | 1.0% | 24 48 | o o | 0 | 5 <u>0</u> | se dev | #120 8/21 |
| | | | NA | NA | | | |
| | Ĺ | 24 | | | | , V 1 | |
| | | 48 | | | | | |

a - Dosage applied by technician indicated
 NA - Not Applicable

| • | DERMAL S | ensttizati | ON STUDY | IN GUINE | PIGS | | | • |
|--------|------------------|------------|------------|-----------|------------|------------------|-------------|--------------|
| | Test Group: | RT No. 8 | 11605 | Vehicle C | 990 saline | Test Material | Vari Lot | 1138 1138 |
| | Positive Control | | | | | | | |
| | imal Received | | | | I | ate Initi | a ted | בגור |
| Source | Dean Dan | Se | × <u>3</u> | | . Ca | allenge D | ate _ | 8/19/ |

| | . | | | | 6 | Reg | |
|------------------------------|---------------------------|-------------------------------------|----------|-------|----------|-------------|----------|
| Sensi- tizing Dose No. | Dose ⁴ (ml) | Obser- vation Period (Rrs) | Erythema | Edema | micies | Recorded By | 981 |
| , 1 | 0.4 | . KA | RA | KA | B | R | 3/02 |
| | 1.0% | 24 48 | 00 | 8 | er JK | W. | 1/23 |
| 2 | 0.4 | NA NA | RA | NA | NOO | M | 7/24 |
| a | 1.0.% | 24 48 | 8 | 8 | KOX | 790 | 7/30 |
| 3 | 0.4 | NA | NA | · NA | R | R | 915 |
| ٦ | 1.0% | · 24 | 00 | 0 | MIN | ER | 810 |
| Challenge | 0.4 | KA | KA | NA | 55 | ER. | e 19 |
| Dose | 1.0% | 24 48 | 0 | 0 | 92 90 | 58 dev | 8 20 |
| | | | NA | NA | | | 2/4 |
| | | 24 48 | | | | | <i>.</i> |

a - Dosage applied by technician indicated
 NA - Not Applicable

| | DERMAL S | INSTITZ. | ATION STUDY | IN GUINEA | PIGS | Took | Vari | soft |
|-------------|------------------|----------|-------------|-----------|------------|------------|--------------------|-----------|
| \boxtimes | Test Group: | RT No. | 871605 | Vehicle o | 990 saline | Material | <u> †ما</u> | 1138 |
| NA | Positive Control | Group _ | NA . | Vehicle | NA | _ Animal N | 641 6. <u>C</u> | 0- 371 |
| Date Ar | nimal Received | 7/10 | 81 | | 1 | Date Initi | a ted | zlaal |
| Source | Dean Day | 1 | Sex · 👌 | | | allenge I | lato | alial |

| | • | | | | e e | les. | |
|------------------------------|---------------------------|-------------------------------------|----------|----------|----------------|------------|------|
| Sensi- tizing Dose No. | Dose ⁴ (ml) | Obser- vation Period (Hrs) | Erythema | Edema | mic ien | ecorded By | 1981 |
| , | 0.4 | MA | KA | , RA | R | R | The |
|) | 1.0% | 24 48 | 8 | | ER JR | W | 7/24 |
| . | 0.4 | NA | NA | NA | NZO | NOO | 7/29 |
| a | 1.0% | 24 48 | 0 | 0 | 100 100 | Da | 7/30 |
| 2 | ب 0 | NA | AK | . NA | R | R | 815 |
| 3 | 1.0% | · 24 | 0 | 0 | AITO FR | MAN) ER | |
| Challenge | 0.4 | XA | KA | NA | ೕ೭ | FR | 8 19 |
| Dose | 1.0% | 24 48 | 0 | <u>ි</u> | 52 90 | ER de | 8/2/ |
| | | XA_ | NA | KA | | ÷' | |
| | | 24 48 | | | · | | |

a - Dosage applied by technician indicated
 NA - Not Applicable

Dermal Sensitization In Guines Pigs - Body Weights

Test Group RT No. 871605 Vehicle 0.990 saline Test Comp NA Positive Control Group NA Vehicle NA

| | - 오 | | | | | | |
|------|-------------|----------------|---------------|----------------|---------------|------|-----|
| | T | 1 | Anima | Number | | | |
| 0419 | 0420 | 6410 - 0421 | 0432 6410- | 6410 - 0423 | 6410- 0426 | 0459 | 041 |
| 393 | 356 | 380 | 378 | 368 | 354 | === | |
| 451 | 399 | 436 | 396 | | | 336 | 40 |
| 500 | 469 | 490 | 440 | 427 | 402 | 389 | 480 |
| 565 | = 11 | | | 495 | 468 | 460 | 57 |
| 417 | | 531 | 481 | 546 | 507 | 489 | 63 |
| 911 | 547 | 565 | 519 | 605 | 555 | 544 | 689 |
| | | | | | | | - 1 |

| | | Animal Number |
|-------|-------|-------------------------|
| 6410- | 6410- | |
| 0431 | 0432 | · |
| 354 | 365 | Scale Used: K.Tron 4809 |
| 391 | 401 | Scale Used: K-TRON 4809 |
| 442 | 459 | Scale Used: K-TRON 4809 |
| 491 | 501 | Scale Used: KTRON 4809 |
| 535 | 560 | Scale Used: K.Ton 4809 |
| - | | Scale Used: |

Dermal Sensitization in Guinea Pigs - Daily Observations Varisoft 475 : Test Group RT No. 871605 Vehicle 0.9% saline est Compound Lot 1138 K

5-

| | Sex | 7 | | | | | | | |
|----------------------|------------------|----------|---------------|---------------|---------------|---------------|---------------|---------------|--------------|
| | <u> </u> | | imal Numi | er | | | | 7 | |
| 6410- 0419 | 0420 | 0421 | 6410- 0422 | 6410- 0423 | 6410- 0426 | 1 | 6410. 0430 | | Data 1981 |
| N | N | N | N | N | N | N | N | 88 | 7/22 |
| N | I N | N | N | N | N | N | N | ER. | 7/23 |
| | N | | N | N | N | ıV | N | 18 | 7/24 |
| N N | N | N | N | N | N | N | N | TP | 7/25 |
| N | N | N | N | N | . N | N | 1 | JR | 766 |
| N | N | N | N | N | N | \mathcal{N} | \mathcal{N} | JR | 7/27 |
| V | N | N | N | N | N | N | Λ/ N | 1/20 | 7/28 |
| N | N | N | ·N) | N | \sim | N | N | NX | 7/29 |
| 4 | N | -1 | J . | 2 | N | N | N | De | 7/31 |
| 7 | 2 | 2 | N | N | N | N | N | | 8/ |
| 2 | 2 | <u> </u> | <i>u</i> | N | N | N | N | Sh | 8/2 |
| 2 | W | 2 | 2 | 2 | <u> </u> | 2 | N | che | 8/3 |
| 1 | N | N | N | N | N | N | 1 | da | 81.4 |
| N | N ₋ - | N | N | N | N | N | N | JP 1000 | 8/6 |
| N | N | N | N | N | N | N | N | FR | 8/7 |
| N. | N | N' | N | N | N | N | N | \mathcal{F} | 8/8 |

N - No Visible Abnormalities

| - | Derma | 1 Sensiti: | estion in | Guines | Pigs - De | ily Obse | | • | f+ 475 |
|-------------|----------|------------|-----------|--------------|--|----------|----------|-----------------|--------|
| \boxtimes | | | | | <u>0.770 sc</u> | linesest | Compound | Lo+ 11 | ++ 475 |
| NA | Positive | Control Gr | dno: | VA | hicle | NA | Room No. | 7 | 20 V |
| | Sex | | | | | | | | |
| 6410 | - 6410- | As | inal No | ber | | | | | |
| | 10432 | | | | | | | Tech- nicies | |
| N | N | | | | | | | | 1981 |
| N | | | | | | | | ER | |
| N | N | | - | | | | | ER | 7/23 |
| | | | - | | - | | | JR | 7/24 |
| N | N | | -+ | | | | | R | 7/25 |
| | | | | _ | | | | JR | 7/26 |
| N | | | | \ | | | | IR | 7/27 |
| N N | | <u>.</u> | | - | | | | NOV | 7/28 |
| l N | \/ | | | | | | | ADA | 7/29 |
| 7 | N | | | | | | | m | 7/30 |
| -N- | | | | | | | | X | 7/3, |
| ม | N | | • | | | | | c L | 8/1 |
| 2 | N | | · | | | | | - m | 8/2 |
| 7 | N | | | | | | | del | 8/3 |
| N | N | | | | | | | del | 8/4 |
| N | N | | | | | | | R | 8K |
| \sim | N - | | | | | | | NUX | 8/10 |
| N | N | | | | | | \ | ER | 8/7 |
| N | N | | | | | | | IR IR | 8/8 |

N - No Visible Abnormalities

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

| | | No. <u>8716</u> 0 | O 5 Vehicle S | | | uVar Lo | isof+ 4 + # 113 |
|-------|-------------------|-------------------------------------|---------------|---------|-----------------|-------------|--------------------|
| | ean Dau | | 8 Sex | Dete I | sitiete | | 7/9/8/ |
| 6410 | Doce ⁴ | Obser- vation Period (Ers) | Erythens | Edems | echnician | Recorded By | 1981 |
| 0318 | 0.5 5.0% | NA 24 48 | NA O | KA O | FP VDQ MR | FR. | 7/9 |
| 03186 | 0.5 | NA 24 48 | NA. | NA C | SE JE WE | se se | 7/19 |

MA

MA

NA

NA

a - Dosage applied by technician indicated NA - Not Applicable
Orecording error 7/9/81 ER

NA

24 48

MA

24 48

MA

24 48

Dermal Sensitization In Guinea Pigs - Body Weights

Naive Naive Stoup RT No. 871605 Vehicle 0.9 % saline Test Compound Lot 1138 Varisoft 4

Positive Control Group NA Vehicle NA

| | | | Animal | Number | | 7 | |
|---------------|----------------------|-------------------------------|---------------------|--------|--|-----------------|-------|
| 6410- 0393 | 6410- 0394 | ८४।०- ०५ २ ५ | 6410- 0425 24 | | | Tech- nician | Da 19 |
| 418 | 374 | 222 | 329 | | | | 19 |
| | | 333 | JQ 1 | | | . عع | 7/: |
| 520 | 452 | 409 | 400 | | | | |
| <i>575</i> | 508 | 475 | | | | NDS | 7/2 |
| | | 110 | 436 | | | اح ز | 8/5 |
| 656 | 577 | 541 | 480 | j | | · 1 | |
| 705 | 638 | 611 | 523 | | | <u> </u> | 8/ |
| | | <u> </u> | <u> </u> | | | ER | |
| | | | _ | | | | _ |

| | Animal Number | | |
|---|--------------------------|-----------------|--------------|
| | · | Tech- nician | Da |
| | Scale Used: K. Tron 4809 | | |
| | Scale Used: K-TRON4805 | εθ | 7 |
| | Scale Used: K-TRON 4809 | OTW | 7/2 |
| | Scale Used: K TROAL HEDG | 18 | 81 |
| | Scale Used: K. Tron 4809 | 50 | 8/1 |
| _ | Scale Used: | ER | 8 10 |

NA - Not Applicable 1) form change 7/20/81 ER Dermal Sensitization in Guines Pigs - Daily Observations

Naive Sterile

Offices Group RT No. 871605 Vehiclea990 Saline Test Compound Lot 1138 K

NA Positive Control Group NA Vehicle NA Room No. 2

| | | As: | imal Numb | er | | | | | |
|----------|---------------|---------------|---------------|----|-----|----------|---------------|-----------------|-----------|
| 0393 | 0410- 0394 | 6410- 0424 | 6410- 0425 | | | | | Tech- nicien | Date 1981 |
| N | N | \sim | \sim | | | | | ER | 7/aa |
| N | N | N | N | | | | | ER. | 7/23 |
| N | ₩. | N | N | | | | | 18 | |
| N. | N | 1/ | N | | \ · | | | ROR | 7/2- |
| N | N | N | N | | 1 | | | 78 | 7/26 |
| N | N | N | N | | _ | | | IR | 7/27 |
| 2 | 1) | \sim | N | • | | | | 97 | 7/28 |
| | N | 2 | N | | | | | 1000 | 7/29 |
| <u>N</u> | N | \sim | N | | | \ | | 740 | 7/30 |
| 2 | 2 | 2 | N | | | | | D | 7/31 |
| I | | | N | | | -+ | | 2 | \$ |
| N | <u>N</u> | Ν | N | | | | | die | 8/2 |
| N | N | N | 2 | | | | | de | 8/3 |
| <i>N</i> | N | | | | | | \ | | 8/4 |
| N | N | N | N | • | | | | 77 | 85 |
| N | N | N | N | | | | \ | | 8/6 |
| N | N | N | N | | | | $\overline{}$ | ER | 8/3 |

N - No Visible Absormalities

Drewiding error

NA - Not applicable

O form change 7/20/81 ER

-(-

Dermal Sensitization in Guinea Pigs - Daily Observations

Naive

Sterile

Offices Group RT No. 871605 Vehiclea990 Saling Test Compound Lot 1/38 K

MA Positive Control Group NA Vehicle NA Room No. 2

| | • | | imal Numb | er · | | - | |
|----------------------------|---------------|---------------|---------------------------------------|------|---|------------------|--------------|
| 0393 | 0410- 0394 | 6410- 0424 | 6410- 0425 | | • | Tech- nician | Date 1981 |
| N | N | N | N | | | R | |
| N | <i>N</i> | N | N | | · | de | |
| 7 2 | 2 | N | N | | | Na | 8/12 |
| <i>N N N N N N N N N N</i> | N | N | مل | | | ER dew | 8/14 |
| N | N | · N | \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ | | · | DR DR | 8/15 |
| N | N | N | | | | da | 8/17 8/18 |
| N | N | N | N | | | EL dw | 8/2C |
| N | N | N | Ñ | | | kw | 8/2 |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |

N - No Visible Abnormalities

NA - Not Applicable

O form change 7/20/81 ER

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Naive Group:

RT No. 871605 Vehicle 0990 soline Material Lot 1138 K

Varisoft 47

| | Dean Do | | sex <u>3</u> 9 | Challe | | | /22/8 8/19/ |
|------------|------------------------|-------------------------------------|----------------|----------|------------|-------------|----------------|
| Asimal No. | Dose ⁴ (ml) | Obser- vation Period (Hrs) | Erythema | Edema | ecimician | Recorded By | 1981 |
| J393 | 0.4 | KA | NA | NA. | 5 2 | 50_ | 8/19 |
| 3 | 1.0% | 24 48 | 0,5 | 0 | ٤٩ | 1 de | 8/20 |
| | | 46 | 0 | _ 0 | ج | de | <u> 8/21</u> |
| 2394 | 0.4 | NA | NA | NA | SE | FR. | 9/19 |
| ð | 1.090 - | 24. | 0 | 0 | ٤٤ | deo | 8/20 |
| | | 48 | 8 | <u> </u> | ٤٤ | del | 8/21 |
| 0424 | 0.4 | . NA | NA | . KA | 50 | 50 | 2/19 |
| 9 | 1.0% | 24 | 0 1 | Ò | FL. | dw | -8/20 |
| <u>_</u> | 1.0 /6 / | 48 | Ð. 1 | 0 | 88 | ace | 8/21 |
| 0425 | 0.4 | KA | KA | KA | SP. | FR | 8/19 |
| \$ | 1.0% | 24 | <u> </u> | O· 1 | ્તરા | ; deu | 18120 |
| | 1.0 6 | 48 | . 0 : | 0 | وفي | 1 des | 18/2/ |
| | | NA. | NA. | NA | ·. | | |
| | 1 | 24 | | | | | 1 |

48

a - Dosage applied by technician indicated NA - Not Applicable

Oform change 7/21/81 EL

Orccording error 7/21/81 EL

Dose Ranze

| Test Grow | ip: RI No | 871605 | Sterile Vehicle 0.9% Saline | Test Material | Varisoft 475 |
|-----------|-----------|--------|--------------------------------|------------------|--------------|
| | | | • | | Lot 1138 K |

Date Animal Received ____5|28|8| Date Initiated $\frac{7/9/81}{}$ Source Dean Daw

| 6410- | | a - | | | ecimi | Recorded | Date |
|--------------|------------------------|-------------------------------------|----------|-------|----------|------------|--------------------------|
| Animal No. | Dose ² (ml) | Obser- vation Period (Hrs) | Esythema | Edema | nician | ted by | i ^a . 1981 |
| 02 <i>77</i> | 0.5 | KA | HA | NA | E.R. | 88 | |
| 0277 A | 1.0% | 24 48 | 0 |) > | MR | 1110 | 7/17 |
| 0277 | 0.5 | NA | NA | NA | γρ. | ER | 17/2 |
| (B) | 5.0% | 24 48 | | 1.0 | JR WR | 5 <u>e</u> | 7110 |
| | | WA | NA | · NA | | i | |
| | | 24 48 | | | | | |
| | | KA | NA | KA | | | |
| | | 24 ! 48 ; | | | , | 1 | • |
| | | MA | NA. | NA | | | |
| | | 24 | | | | | |

a - Dosage applied by technician indicated
 NA - Not Applicable

Head

Tail

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

| rest Group: | RT No. 27 | 11605 Venicle | Sterile 0.9 Mater: | Les Varisoft 4 |
|------------------|-------------|---------------|--------------------|----------------|
| | .11 1- | | Solur | LOT 1138 |
| Date Animal Rece | ived 4/10/8 | | • | · |
| Source Dean | nul | Sex | Date Initiat | ed (1/22/81 |

| 14110 | 1 | | | | Tech | Reco |
|--------------------------------|----------------------------|-------------------------------------|--------------|---------|--------|---------------|
| 6410 - ARITEL NO. (Gite) | Dose ⁴ (Ml.) | Obser- vation Period (Hrs) | Erythems | Idens | nician | Hecorded by |
| 0251 | 0,5% | NA | NA. | NA | DEG | NDP 6122 |
| (a) | 2-01 | 24 | 1.0 | O | 3 | |
| | 25% | 48 | 1.0 | 1,0 | I ACTO | 109 6/24 |
| 0251 | 0.5 | NA | NA | NA | Ray | N501622 |
| 8 | 5090 | 24 | 3.0 | 1 3.0 | 7.7 | -N 6/23 1 |
| | 70 10 | 48 | 3.0 | 3.0 | 1/30 | W7 10174 |
| 0251 | 0.5 | · · NA | NA | · NA | NJO | NDU MSS |
| (C) | 7500- | 24 | 3.0 | 3.0 | H | S 4/23 |
| | 1900 | 48 | <i>3</i> , 0 | 13.0 | 1120 | AED INZU |
| 0251 | 0.5 | NA | NA | NA | 100 | SSPIRCA |
| ! (מ) ! | INDOL - | 24 1 | 3.0 3.0 | 3.0 | 700 | JY 1993 |
| | 11717-10 | 48 | <i>3</i> . 0 | · . ३.० | (12) | 11579 11/0/24 |
| | | NA | XV. | NA | | |
| | 1 | 24 | | | | |
| | Danadi E | 48 | | | | |

Ormanding Error 4/22/81 ME

a - Dosage applied by technician indicated

| • | DERMAL S | ENSITIZATI | ON STUDY | IN GUINE | A PIGS | | | ٥. |
|---------|------------------|------------|-----------|-----------|------------------------|------------------|-------------|--------------|
| X | Test Group: | RT No. 8 | 71605 | Vehicle | Sterile 0.9% saline | Test Material | Vari Lot | 1138 1138 |
| NA | Positive Control | Group | NA_ | _ Vehicle | NA | _ Animal No | ٠ <u>٥</u> | 451. 0- |
| Date Ar | mimal Received | 7/10/8 | 1 | _ | 1 | Date Initia | ted | 7/22 |
| Source | Dean Day | 1 s | <u> 우</u> | | Q | ellenge De | Lte | 21191 |

| | | | | , | iec: | lec | L |
|------------------------------|---------------------------|-------------------------------------|----------|-------|--------|-------------|--------------|
| Sensi- tizing Dose No. | Dose ^a (ml) | Obser- vation Period (Rrs) | Erythema | Edena | nician | Recorded by | 981 |
| 1 | 0.4 | RA | NA. | KA | R | SP | 7/22 |
| | 1.0% | 24 48 | 0 | 0 | و ا | ME | |
| 2 | 0.4 | NA | NA. | NA | Pan | 1000 | 7/29 |
| ょ | 1.0% | 24 . 48 | 0 | 0 | 700 | 10 | 7/30 7/34 |
| 2 | 0.4 | NA | NA | NA | 13 | T | 8K |
| റ | 1.0% | · 24 | 0 | 0 | NDX) | NX | |
| Challenge Dose | 0.4 | NA | NA. | NA | 58 | FR | 8 19 |
| Dose | 1.0% | 24 48 | 0 | 0 | ۶۶ | ER AU | 8/20 8/2/ |
| | | -XA | NA | KA | | # 1 | |
| | | 24 48 | | | | | |

a - Dosage applied by technician indicated
 NA - Not Applicable

| DE | RMAL SENSITIZAT | ION STUDY IN GU | INEA PIGS | Vanicas | ب ب |
|-------------------|-----------------|-----------------|---|--------------------------------|----------|
| Test Group | : RT No. 8 | 371605 Vehic | INFA PIGS Sterile Te ile 0.9% saline Me | st terial Lot 113 | a K |
| NA Positive C | control Group | NA Veni | cle NA A | 6410- nimal No. <u>0</u> 년3 | ià |
| Date Animal Recei | ved 7 10/8 | 31 | Dat | e Initiated 7/2 | <u> </u> |
| Source Doon | David | Sex P | . Chal | lenge Date 81 | 9 8 |

| | • | | | | Tech | Res | L |
|------------------------------|---------------------------|-------------------------------------|----------|-------|----------|-------------|-------------|
| Sensi- tizing Dose No. | Dose ^a (ml) | Obser- vation Period (Hrs) | Erythema | Edema | nician | Recorded By | 1 81 |
| | 0.4 | KA | RA | NA | R | TP | 7/22 |
| , | 1.0% | 24 48 · * | 0 | .0 | 66 JK | MR | |
| | - 0. 4 | MA | RA | NA | PCU | ND | 7/29 |
| a | 1.0% | 24 . 48 | 0 | 0 | KDD | 772 | 7/30 |
| | 0.4 | NA | AK | NA | R | R | 86 |
| 3 | 1.0% | · 24 | | 0 | NOX) | N7X) FP | |
| Challenge Dose | 0.4 | KA | NA. | NA | 50 | ER. | 8 19 |
| Dose | 1.0% | 24 48 | 0 | 0 | 5 P | ES! | 8/21 |
| | | | NA | NA | ., | ÷ | |
| | | 24 48 | | | | | |

a - Dosage applied by technician indicated NA - Not Applicable

| | DERMAL S | ENSITIZATION | STUDY | IN GUINE | A PIGS | | Vario | 64 |
|-------------|------------------|--------------|-------|----------|------------------------|------------------|-------------|------------|
| \boxtimes | Test Group: | RT No. 871 | 605 | Vehicle | Sterile 0.9% saline | Test Material | <u>Lo</u> + | 1138 K |
| | Positive Control | | | | | | 6410 |) - |
| Date A | nimal Received | 7/10/81 | | | ; | Date Initi | a ted | 7/22/ |
| Sau = 22 | Donation | 1 50- | Q | | a | nallanea D | | aliais |

| | • | | | | rec L | lec | 2 |
|------------------------------|------------------------|-------------------------------------|----------|-------|------------|-------------|--------------|
| Sensi- tizing Dose No. | Dose ^a (ml) | Obser- vation Period (Rrs) | Erythema | Edema | nician | lecorded by | 1981 |
| | o. 1 | RA | KA | HA | R | R | 7/22 |
| 1 | 1.0% | 24 48 | 0 | 0 | ER | WS JK | 7/23 |
| | 0.4 | MA | NA | NA | 120 | 120 | 7/29 |
| 2 | 1.0.% | 24 . 48 | 0 | 0 | KOKO DA | 740 | 7/30 |
| 2 | 0.4 | MA | NA | KA | R | 57 | BK |
| 3. | 1.0% | . 24 48 | 0 | 0 | NTX) | NX) FR | <i>81</i> 0 |
| Challenge | 0.4 | NA | NA | NA | જ | ۶۶ | e l e |
| Dose | 1.0% | 24 48 | 0 | 0 | er Er | 58 | 8 70 8/21 |
| | | | MA | KA | | ÷ | |
| | | 24 48 | | | | | |

a - Dosage applied by technician indicated
 NA - Not Applicable

| | DERMAL S Test Group: | ensitization rt no. 871 | 518BY 1 | N GUINEA PI Ster enicle 0.9% | ics rile I saline M | est aterial L | arisoft 4 ot 1138 K |
|---------|----------------------|----------------------------|---------|------------------------------------|---------------------------|------------------|------------------------|
| NA | Positive Control | | | | | (| 6410- |
| Date Ar | nimal Received | 7/10/81 | | • | Da | te Initiat | ed 7/22/8 |
| Source | Dean Day | 1 Sex | <u></u> | - · | Cha | llenge Dat | 8 19 81 |

| | • | | | | i ec | Rec | |
|------------------------------|-------------------|-------------------------------------|----------|-------|------------|-------------|---------------|
| Sensi- tizing Dose No. | Dose ⁴ | Obser- vation Period (Hrs) | Erythema | Edena | Technician | Recorded By | 1981 |
| | 0.4 | KA | NA | KA | R | R | 7/22 |
| | 1.0% | 24 48 | 0 | | ER | MP JK | L7/23 |
| | ٠ ن | NA | МА | HA | NZO | 1200 | 7/29 |
| 2 | 1.0% | 24 48 | 0 | 8 | 100 | 77 | 7/30 |
| 2 | 0.4 | NA | NA | NA | R | R | 85 |
| 3 | 1.0% | 24 48 | 0 | 0 | NXV EP | MX) | 810 |
| Challenge | 0.4 | NA | RA | NA | ೯೭ | EE. | el 18 |
| Dose | 1.0% | 24 | 0.5 D | 0 | 5 <u>6</u> | 58 Hal | 8 20 \$/2/ |
| | | | MA | NA | | 4 | |
| | | 24 48 | | | | | |

a - Dosage applied by technician indicated
 NA - Not Applicable

| DERMAL S | ENSITIZATION | STUDY | IN GUINEA | PIGS | | Va = i | · ~ C + |
|----------------------|--------------|-------|-------------|---------------------|------------------|------------------|--------------------|
| Test Group: | RT No. 87 | 1605 | Vehicle 0.5 | terile 1% saline | Test Material | <u>+ما</u> | 1138 K |
| NA Positive Control | Group | NA | _ Vehicle _ | NA | _Animal h | 2 . • | o-@ 글 O닉 |
| Date Animal Received | 7/10/81 | | | | Date Initi | | 1 , |
| Source Doon Door | 1 Sex | 2 | | · a | ballenge I | Date | 8/19/8 |

| | | | | | Hech | Reco | = |
|------------------------------|---------------------------|-------------------------------------|----------|--------|------------|-------------|--------------|
| Sensi- tizing Dose No. | Dose ⁴ (ml) | Obser- vation Period (Hrs) | Erythema | Ed ema | nician | Recorded By | 981 |
| | 0.4 | RA | KA | KA | R | R | 7/22 |
| | 1.0% | 24 48 | 8 | 0 | SE JP | NYC III | 7/22 |
| | 0.4 | NA | NA | АЙ | NON | 1000 | 7/29 |
| 2 | 1.0% | 24 48 | CC | 00 | 100 | 720 | 7/30 7/31 |
| 2 | 0.4 | NA | NA | Na | R | 37 | 815 |
| 3 | 1.0% | 24 48 | 0 | 0 | 1/2X) | NOD FR | <i>810</i> |
| Challenge | 0.4 | KA | NA | NA | وع | ER | 8/19 |
| Dose | 1.0% | 24 48 | 0 100 | 0 | 5 <u>P</u> | ER. | 8/21 |
| • | | - XA | NA | NA | ., | # . | , |
| - | | 24 48 | | | | | |

a - Dosage applied by technician indicated
NA - Not Applicable

Orecording error 8 20 8 1 50

N

NA

NA

NA

NA

0

| . Test | <u>DERMAL</u> : Group: | • | 1605 Vehic | Sterila |
|------------------------------|---------------------------|-------------------------------------|------------|---------|
| NA Post | itive Coutro | ol Group | NA Vehi | cleNA |
| | _ | 7/10/81 | <u> </u> | |
| | | | | |
| Sensi- tizing Dose No. | Dose ⁴ (ml) | Obser- vation Period (Rrs) | Erythema | Edena |
| Sensi- tizing | Dose* | Obser- vation Period | | |

NA

24

48

NA

24 48

NA 24

48

24 48 NA O

0

NA

0.5

MA

0

a - Dosage applied by technician indicated
 NA - Not Applicable

0.4

1.0%

0.4

1.0%

0.4

1.0%

Challenge

Dose

| | DERMAL S | ENSITIZATION | STUDY | IN GUINEA | PIGS | | | ر م |
|--------|---|--------------|-------|-------------|------------------------|------------------|------|-----------|
| | Test Group: | RT No. 87 | 605 | Vehicle o | sterile 1990 saline | Test Material | Lot | 1138 H |
| | Positive Control | | | | | | 6419 | 0- |
| Date A | nimal Received | 7/10/81 | | | . I | Date Initi | ated | 7/22/ |
| C | $\mathcal{T}_{\cdots}\mathcal{T}_{\circ}$ | 1 5 | 2 | | ~ | alleman D | | aliala |

| | 1 | | | | iec E | Rec | |
|------------------------------|---------------------------|-------------------------------------|----------|-------|----------|-------------|------|
| Sensi- tizing Dose No. | pose ⁴ (ml) | Obser- vation Period (Rrs) | Erytheme | Edema | nician | Recorded By | 981 |
| | 0.4 | KA | NA. | NA | R | R | 7/22 |
| | 1.0% | 24 48 | . 0 | 00 | EK IR | MR | 777 |
| | 0.4 | NA | NA | NA | 120 | 120 | 7129 |
| 2 | 1.0% | . 24 48 | 8 | 8 | NO. | 174 | 7/30 |
| 2 | 0.4 | NA | NA. | . NA | R | TH | 3/5 |
| 3 | 1.0% | . 24 48 | O O | 0 | NOW | NOTO | 817 |
| Challenge | 0.4 | NA | NA | NA | ER | EQ | 9119 |
| Dose | 1.0% | 24 48 | 0 | 0 | 93 | FR | 8/2/ |
| | | *** | NA | NA | | 41 | |
| | · | 24 48 | | | | | |

a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUT

| \boxtimes | Test Group: | RT No. 8 | 71605 | Vehic |
|-------------|------------------|----------|--------------|--------|
| NA | Positive Control | Group | NA | _ Vehi |
| Date A | nimal Received | 7/10/ | 81 | |
| Source | Dean Day | 1 | iex <u> </u> | |

| Sensi- tizing Dose No. | Dose ^d (m1) | Obser- vation Period (Hrs) | Erythems |
|------------------------------|---------------------------|-------------------------------------|----------|
| | 0.4 | RA | NA |
| | 1.0% | 24 48 | 9 |
| | 0.4 | KA | NA |
| 2 | 1.0.% | 24 | 00 |
| 2 | 0.4 | NA | AK |
| 3 | 1.0% | 24 | |
| Challenge Dose | | NA | . NA |
| Dose | 1.0% | 24 | 0 |
| | | NA. | NA |
| | | 24 | |
| |] | 48 | |

a - Dosage applied by technician indicated
 NA - Not Applicable



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A Division of Raiston Purina Company

EFFORT

MA FORFTI L. HARRISON SHEREY CHEMICAL COMPANY, INC. P.O. 1971 546 DUBLIN, OH 48017

RT LAR NO. 871606

ENTERED 06/16/81

REPORTER 09/18/81

'ARIS'TT 475: 107 1104K

TECHASE OFDER NUMBER 021-49378

'LOSED:

DFRMAL SENSITIZATION STUDY IN GUINEA PIGS

'MODIFIED CLOSED PATCH TECHNIQUE) - METHOD, SUMMARY

RAW DATA ATTACHED

TICHED:

THOMPTON, BS

MANAGER, ACUTE TOXICOLOGY

BY AND HOR BALIECH SCIENTIFIC SERVICES, INC.



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11 MUMPER 271606

FAGF 2

777 475: IDT 1104K

TENSITIEATION

POTIVE: TO DETERMINE THE DELAYED CONTACT HYPERSENSITIVITY POTENTIAL OF TEST MATERIAL IN GUINEA PIGS.

ANDIAL: TWENTY-FOUR ACCLIMATED GUINEA PIGS, WEIGHING FROM 324 TO 416 GREE USED FOR THIS SIUDY. THE ANIMALS WERE DIVIDED INTO TWO CROUPS TONSISTING OF A NAIVE CONTROL GROUP OF FOUR GUINEA PIGS AND A TREATED GROUP OF TWENTY GUINEA PIGS. AN EQUAL NUMBER OF MALE AND FEMALE ANIMALS WERE LACED IN EACH GROUP. THE ANIMALS WERE IDENTIFIED BY ANIMAL NUMBER AND LAGED IN SCREEN-BOTTOM CAGES IN THE ANIMAL WERE INDIVIDUALLY HOUSED IN SCREEN-BOTTOM CAGES IN TEMPERATURE AND HUMIDITY CONTROLLED BOOMS. THE ANIMALS WERE PROVIDED CONTINUOUS ACCESS TO PURINA GUINEA PIG CHOW AND WATER THROUGHOUT THE STUDY ERIOD.

TPARATION OF TEST MATERIAL: TO PREPARE A 1.0% WEIGHT/VOLUME MIXTURE, 1.0 G F VARISCET 475: LOT 1104K WAS WEIGHED INTO AN ERLENMEYER FLASK. STERILE 1.9% SALINE WAS ADDED TO MAKE A TOTAL VOLUME OF 100 ML. THE MIXTURE WAS THEN STIRRED USING A STIR PLATE AND A MAGNETIC STIR BAR TO A UNIFORM TUSPENSION. THE TEST MATERIAL WAS PREPARED FRESH PRIOR TO EACH APPLICATION.

ATMENT: THE DAY BEFORE EACH APPLICATION THE HAIR WAS REMOVED FROM THE GHOVEDER OF EACH ANIMAL WITH ELECTRIC CLIPPERS. THE TEST MATERIAL WAS FIRD TO DAY AREA ON EACH ANIMAL BY PLACING 0.4 ML OF THE FRESHLY PREPARED TEST SUBSTANCE ON A WEBPIL PAD (7/8 INCH X 1 INCH) AND PLACING THE PAD ON THE DEST SITE ALONG THE MIDLINE OF THE BACK. THE PATCH WAS COVERED WITH THE MABBER DAY AND SECURED WITH AN OVERWRAP OF ELASTOPLAST TAPE. THE DRESSING THAT IN PLACE FOR A PERIOD OF SIX HOURS AT WHICH TIME IT WAS REMOVED. HE TEST MATERIAL WAS REMOVED BY A GENTLE RINSE WITH WARM WATER BEFORE STUFNING THE ANIMALS TO THEIR CAGES.

THE ANIMALS RECEIVED ONE APPLICATION PER WEEK FOR THREE WEEKS FOR A TOTAL THREE APPLICATIONS.

HALLENGE DOSE AT A VOLUME OF 0.4 ML WAS ADMINISTERED TO THE TEST GROUP IN THE JAME MANNER AS DUPING THE SENSITIZING PHASE OF THE STUDY. AT THIS TIME, THE FOUR NAIVE (SEEVIGUSLY UNTREATED) CONTROL ANIMALS WERE ALSO TREATED ITH A CHALLENGE APPLICATION. THE CHALLENGE APPLICATIONS WERE MADE TO A LESHLY CLIPPED SKIN SITE THAT HAD NOT BEEN PREVIOUSLY TREATED. TWENTY-FOUR DURS AFTER SRIMARY CHALLENGE, THE ANIMALS WERE DEPILATED WITH NEET CREAM AIR SEMOVER (WHITEHALL LABORATORIES, INC., NEW YORK). THE DEPILATORY AS ASPLIED ON THE TEST SITES AND SURROUNDING AREAS FOR 30 MINUTES. THEN DEPILATORY WAS THOROUGHLY WASHED OFF WITH WARM WATER, THE ANIMALS FIED WITH A TONEL AND RETURNED TO THEIR CAGES.



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THE KYMBER 971606

PAGE 3

CHRISTED 455: LOT 1104K

TYIN CHASIDIDATION (COMMINUED)

CREEVATIONS: THE APPLICATION SITES WERE READ AND SCORED FOR FRYTHEMA AND EDEMA AT 14 AND 45 HOURS FOLLOWING EACH APPLICATION DURING THE SENSITIZING PRASE OF THE STUDY. REACTIONS TO THE CHALLENGE DOSE WERE READ AND SCORED TWO HOURS AFTER DEPILATION AND 24 HOURS LATER (48 HOUR SCORES). THE ANIMALS AFAE OBSURVED FOR GENERAL BEHAVIOR AND APPEARANCE ONCE DAILY DURING THE ENTIRE STUDY FERIOD. BODY WRIGHTS WERE TAKEN AT STUDY INITIATION AND ATWEEKLY INTERVALS DURING THE STUDY.

BECAUSE ONE ANIMAL (NO. 64100402) EXHIBITED A POSSIBLE SENSITIZATION
RESPONSE TO THE CHALLENGE DOSE, A RECHALLENGE WAS CONDUCTED ON THIS ANIMAL
7 DAYS AFTER THE FRIMARY CHALLENGE. THE SENSITIZED ANIMAL (NC. 64100402,
MALE), ALONG WITH 4 NAIVE CONTROL (ONCE CHALLENGED) ANIMALS, WERE TREATED
WITH 0.4 ML OF RT # 871605 (VARISOFT 475, LOT 1138K) AND 0.4 ML OF
E1 # 871607 (VARISCET 475, LOT 195+136) IN THE SAME MANNER AS FOR THE
REIMARY CHALLENGE RECCEDURE, INCLUDING DEPILATION AND 24 AND 48 HOUR SCORES.

PATHOLOGY: AT STUDY TERMINATION ALL ANIMALS WERE EUTHANATIZED AND DISCARDED.



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148 TUMPET 971606

11819 92 475: 10T 1104K

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KIN DENTIFICATION (CONTINUED)

TEST ANIMAL: GUINER FIGS

SOURCE: DEAN DAUL, LUNEMBURG, WI

DATE ANIMALS RECEIVED: 7/10/81

DATE TEST UNASTED: 7/22/81 DATE TEST COMPLETED: 8/28/81

CUMMARY OF SKIN REACTTONS**

TEST GROUP - MALES

| | ISE | CHALLENGE PHASE | | | | | | | |
|-------------------|-------|-----------------|--------|--------|--------------------|--------|------|--------|--|
| | TH | REE APFI | ICATIO | NS | SINGLE APPLICATION | | | | |
| ANIMAL | ERY | THEMA | ED | EMA | ERY | THEMA | ED | EMA | |
| NUMPER | AVE. | (HIGH) | AVE. | (HIGH) | AVE. | (HIGH) | AVE. | (HIGH) | |
| 64100397 | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | |
| 64100399 | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | |
| 64100400 | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | |
| 64100401 | 0.0 | (0) | 3.0 | (0) | 0.0 | (0) | 0.0 | (0) | |
| 54105452 | 0.0 | (O) | 0.0 | (0) | 0.0 | (0) | 0.5 | (1) | |
| 54100403 | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | |
| 541∩0404 | 9.0 | (0) | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | |
| 54100405 | 0.0 | (0) | 0.0 | (0) | 0.0 | (C) | 0.0 | (0) | |
| 10040€ | 0 • ú | (0) | C . O | (0) | 0.0 | (0) | 0.0 | (0) | |
| 5 41 00407 | 0.0 | (C) | ೧.0 | (0) | 0.0 | (0) | 0.0 | (0) | |
| | | | | | | | | | |
| | | | | | | | | | |
| | | | | | | | | | |

| ΥA | I | ٧ | Ε, | CONTR |)L |
|----|---|---|----|-------|----|
| | | | | | |

| BALT BOATES E | | | | | |
|------------------|-----------|-----|-------|-----|-----|
| 64100378 | UNTREATED | 0.3 | (0.5) | 0.0 | (0) |
| ~ G 3 3 0 | UNTREATED | 0.0 | (0) | 0.0 | (0) |

THE AVERAGE ERYTHENA AND EDEMA VALUE IS THE MEAN SCORE FOR THE SIX OBSERVA-TIONS (SENSITIZING THEATMENT) OR TWO OBSERVATIONS (CHALLENGE TREATMENT) OF THE APPLICATION SITE FOR EACH ANIMAL. THE HIGH READING IS THE HIGHEST SCORE RECORDED FOR THE RESPECTIVE ANIMAL DURING THAT PHASE OF THE STUDY.



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* LAB YTMBER - #71606-

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'ARISOFT 475: LOT 1104K

IKIN OFFRITTICATION (CONTINUED)

TEST ANIMAL: GUINEA FIGS

COURCE: DEAN DAUL, LUMEMPURG, WI

DATE AMINALS RECEIVED: 7/10/81

DATE FOR STARTED: 7/22/81 DATE TEST COMPLETED: 8/28/81

SUMMARY OF SKIN REACTIONS** (CONT.):

TEST GROUP - FEMALES

| | S | FNSITIZI | NG PHA | SE | CHALLENGE PHASE | | | | |
|-------------------|------|----------|---------|--------|--------------------|--------|------|--------|--|
| | TH | BEE APPL | .ICATIO | NS | SINGLE APPLICATION | | | | |
| ANIMAL | EPY | THEMA | ED | EMA | ERY | THEMA | ED | EMA | |
| NUMBER | AVE. | (HIGH) | AVE. | (HIGH) | AVE. | (HIGH) | AVE. | (HIGH) | |
| 4100427 | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | |
| 4100447 | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | |
| 64100409 | 0.0 | (0) | 0.0 | (0) | 0.3 | (0.5) | 0.0 | (0) | |
| 64100411 | 0.0 | (0) | 0.0 | (C) | 0.3 | (0.5) | 0.0 | (0) | |
| 64100412 | 0.3 | (0) | C •O | (0) | 0.0 | (0) | 0.0 | (0) | |
| 54100413 | 0.0 | (0) | C .O | (0) | 0.0 | (0) | 0.3 | (0) | |
| 54100414 | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | |
| 5410041E | 0.0 | (3) | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | |
| 100415 | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | |
| 4100443 | 0.0 | (0) | 0.0 | (C) | 0.0 | (0) | 0.0 | (0) | |
| ALVE CONTROL | | | | | | | | | |
| 64100410 | | UNTR | EATED | | 0.0 | (0) | 0.0 | (0) | |
| 64 1 0040° | | | EATED | | 0.0 | (0) | 0.0 | (0) | |

^{**}THE AVERAGE ERYTHEMA AND EDEMA VALUE IS THE MEAN SCORE FOR THE SIX OBSERVA-TIONS (SENSITIZING TREATMENT) OR TWO OBSERVATIONS (CHALLENGE TREATMENT) OF THE APPLICATION SITE FOR EACH ANIMAL. THE HIGH READING IS THE HIGHEST SCORE RECORDED FOR THE RESPECTIVE ANIMAL DURING THAT PHASE OF THE STUDY.



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LAP TUMBER E71606

TARISOTT → 75: LOT 1104K

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CRIN SENSITIFATION (CONTINUED)
RESULTS:

GENERAL MEHAVIOR AND APPEARANCE: ALL OF THE GUINEA PIGS USED IN THIS STUDY AFFEARED NORMAL THEOUGHOUT THE STUDY PERIOD. NORMAL BODY WEIGHT GAINS WEIGH RECORDED FOR ALL ANIMALS DURING THE COURSE OF THE STUDY.

SKIP REACTIONS TO VARIORT 475: LCT 1104K (1.0% W/V AQUEOUS): ONE MALE ANIMAL (NO. 84100402) RESPONDED TO THE CHALLENGE APPLICATION WITH A SLIGHT EDEMA REACTION AT THE 24 HOUR OBSERVATION. TWO FEMALE ANIMALS (NOS. 6410-3409 AND 64100411) REACTED TO THE CHALLENGE DOSE WITH A VERY FAINT NONCONFLUENT ERYTHEMA AT THE 24 HOUR OBSERVATION.

ONE MALE ANIMAL IN THE NAIVE CONTPOL (NO. 64100378) EXHIBITED A VERY FAINT EPYTHEMA REACTION AFTER RECEIVING 0.4 ML OF THE 1.0% W/V MIXTURE OF TEST NATERIAL.

THE SKIN REACTIONS IN THE TWO TREATED FEMALES WERE NOT GREATER THAN THE SEACTION SEEN IN THE MAIVE CONTROL ANIMALS AND ARE THEREFORE NOT CONSIDERED STUSITIZATION RESPONSES. THE REACTION OF THE ONE TREATED MALE WAS GREATER THAN THE REACTION SEEN IN THE CONTROL ANIMALS AND INDICATES SENSITIZATION.

BECAUSE ONE ANIMAL (NO. 64100402) DID EXHIBIT A SENSITIZATION RESPONSE TO THE CHALLENGE DOSE, A RECHALLENGE WAS CONDUCTED ON THIS ANIMAL AND FOUR NAIVE CONTROL (ONCE CHALLENGED) ANIMALS SEVEN DAYS FOLLOWING THE PRIMARY CHALLENGE.

FOR THE RECHALLENGE DOSE, THE TEST MATERIALS (VARISOFT 475, LCT 1138K AND VARISOFT 475, LOT 195-136, 1.0% W/V AQUEOUS SUSPENSIONS OF EACH) WERE APPLIED TO ONE TEST SITE EACH ON THE TEST AND NAIVE CONTROL A MIMALS. NONE OF THE ANIMALS RESPONDED TO THE RECHALLENGE DOSE WITH ANY SENSITIZATION REPACTION AT EITHER OF THE OBSERVATION PERIODS.

CONCLUSION:

BECAUSE THE INCIDENCE OF A SENSITIZATION RESPONSE OCCURRED IN ONLY 5% OF THE TREATED ANIMALS (1 OF 20), THIS TEST MATERIAL IS NOT CONSIDERED A STRONG SKIN SENSITIZER.

Dermal Sensitization In Guinea Pigs - Body Weights

Test Group RT No. 871606 Vehicle 0.9% saline Test Compound Lot 1104K

NA Positive Control Group NA Vehicle NA

| Sex | 3 | | | | | | | | |
|-------|-------|-------|--------|--------|-------|-------|--------|--------|--------------|
| | | | Animal | Number | | | | Ī | |
| 6410- | 6410- | 6410- | 6410- | 6410- | 6410- | 6410- | 6410 - | Tech- | |
| 0397 | 0399 | 0400 | 0401 | ०५०२ | 0403 | 0404 | 0405 | nician | Date 1981 |
| 402 | 400 | 346 | 357 | 409 | 384 | 416 | 359 | ER | 7/32 |
| 478 | 498 | 432 | 426 | 484 | 460 | 496 | 410 | NOS | 7/29 |
| 537 | 579 | 490 | 490 | 562 | 537 | 580 | 473 | JR | 8/5 |
| 623 | 668 | 554 | 538 | 634 | 614 | 686 | 566 | Z | 8/12 |
| 707 | 737 | 597 | 587 | 697 | 696 | 708 | 618 | · ER | P1 8 |
| | | | | | | | | | • |

| | | Animal Number | T | |
|-------|-------|--------------------------|-----------------|--------------|
| 6410- | 6410- | | | |
| 0406 | Гоно | | Tech- nician | Date 1981 |
| 387 | 382 | Scale Used: KiTron 4809 | se. | 7/22 |
| 462 | 469 | Scale Used: K-Tron 4809 | | 7/29 |
| 548 | 534 | Scale Used: K-Tron 4809 | IR | 8/5 |
| 637 | 598 | Scale Used: K TRON 4809 | De | 8/12 |
| 693 | 643 | Scale Used: K. Tron 4809 | ER. | 8 19 |
| | _ | -Scale Used: | | |

Dermal Sensitization in Guines Pigs - Daily Observations Varisoft 475
Sterile
Test Group RT No. 871606 Vehicle 9% saline Test Compound Lot 1104 K
Positive Control Group, NA Vehicle NA Room No. 2

NA

1

Animal Number 6410-6410-6410-6410-6410-6410-6410-6410-Technicien Date 0397 C400 0399 1040 0402 0403 20404 0405 1981 Maa N Ν Ν Ν ER. 723 Ν N N M N N ER N N M N Ν N N N 7/24 18 JP 7/25 N N N N N 1 N 7/26 حآار 7/27 N N Ν 7/28 N N N N N N 7/29 N N N N NOO 7130 N N 7/31 N Δ λ 8/1 10 N 2 2 N N N 2 N 8/2 N do 2 8/3 2 N N 2 \sim S N ٨ 8/4 N C) N 8/j N N M 816 N M 8/7 Ν N ER N N Ν M 3/9

N - No Visible Abnormalities

Dermal Sensitization in Guinea Pigs - Daily Observations Varisoft 475 Test Group RT No. 871606 Vehicle 0990 salineTest Compound 10+ 1104 K MA Positive Control Group NA Vehicle NA Room No. 2 Sex 8 Animal Number 6410-6410-Tech-7040 000 nicien Date 1981 \mathcal{M} Ν 7/22 ER N Tlas ER. 7/24 7/25 1/26 N 7/21 7/28 N N 7/29 N 7/30 120 7/31 8/1 N N deh 2 3 8/5 N_{-} 80 N 7/8

N - No Visible Abnormalities

Dermal Sensitization in Guinea Pigs - Daily Observations Varisoft 475 Test Group RT No. 871606 Vehicle 9% soline Test Compound Lot 1104 K MA Positive Control Group NA Vehicle NA Room No. 2 Sex & Animal Number 6410-6410-6410- 6410- 6410-6410-6410-6410-Tech-7950 0399 0400 0401 0402 0404 0405 nician Date 0403 1981 8/9 N N N da 8/10 N M N N 7 8/11 IR. 8/12 لم N N N 8/13 N N N N. N ER Ŋ N N \mathcal{N} N 8/16 8/17 8/18 N 8/19 N N N N N N ER فر N N N dev 8/20 N N N N S N S dw 8/21

N - No Visible Abnormalities

| Dermal Sensitization in Guines Pigs - Daily Observations Sterile Varisoft 475 | | | | | | | | | | | |
|---|----------------|----------|--------------|-----------|-----------------------|-----------|---------|-----------------|---------------|--|--|
| X r | est Group | RT No. 8 | 371606 | Vehicle (| sterile 0.990 sali | neTest Co | pound · | Lot 1104 | 7 7 /3 1 K | | |
| | • | | onb <u>N</u> | | | | | | | | |
| | ex C | | | | | <u> </u> | | | | | |
| | | An | imal Numbe | er | | | | 7 | | | |
| ì | 6410- 0407 | \ | | | · | · | | Tech- nicien | Date 1981 | | |
| N | N | | | | | | | R | 8/9 | | |
| W | <i>\lambda</i> | | | | | | | de | 8/10 | | |
| N | N | | | | | | | IR | 8/11 | | |
| N | N | | | | | | | ER | 8/12 | | |
| N | N | | | | | | | ER | 8/13 | | |
| U | h | | | 1 | | | | <u>U</u> | 8/14 | | |
| N | N | | | | • | | | Sa | 8/15 | | |
| N | N | | | | | | | JR | 3116 | | |
| 7 | N | | | | | | | day | 8/17 | | |
| 2 | N | | | | | | | DR | 8/18 | | |
| N | N | | | | | | | ٤٤ | 9/19 | | |
| N | N | | · | | | | | dw | 8/20 | | |
| 1/ | 6 | | | | | | | kos | 8 hl | | |
| | | , | | | | | | | | | |
| | | | | | | | | | | | |
| | | | | | | | | | | | |
| | | | | | | | | | | | |
| | | | | | | | | | | | |

N - No Visible Abnormalities

| | DERMAL | SENSITIZATION | STUDY IN | GUINEA | PIGS | _ | Vari | soft 1 |
|-----------|------------------|---------------|----------|-----------------|-----------------|---------------------|-------------|--------------------|
| \bowtie | Test Group: | RT No. 8711 | 00 v | Ste enicle a | 17618 996.sa | Test LIOMaterial | Lot 6410 | <u>1104</u> K - |
| NA | Positive Contro | 1 GroupNA | | Vehicle . | NA | Animal N | • | |
| Date A | nimal Received _ | 7/10/81 | | | | Date Initi | | - |
| | Dean Day | , \ Sex | 3 | _ | • | Challenge I | Date | 8/19/81 |

| | 4 | | | | | Reco | Da |
|------------------------------|---------------------------|-------------------------------------|----------|-------|------------|-------------|---------------|
| Sensi- tizing Dose No. | Dose ² (ml) | Obser- vation Period (Hrs) | Erythema | Edema | | Recorded By | 1981 |
| | 0.4 | AR | NA | NA | 50 2007 | <u> 60</u> | 7/22 |
| | 1.0% | 24 48 | CO | 0 | Me Il | 5P | 7/23 7/124 |
| | Ċ Ċ | NA | NA | NA | NOW | 1000 | 7129 |
| 2 | 1.0% | 24 48 | 0 | 0 | Dr. | 18 | 7/34 |
| | 0.4 | NA | NA | NA | P | R | 815 |
| 3 | 1.0% | · · 24 48 | 0 | | ER. | NOV | |
| Challenge | | NA | NA. | NA | 8.6 | 50 | 8/20 |
| Challenge Dose | 1.090 | 24 48 | 8 | 0 | 56 56 | de | 8/21 |
| | | *** | NA | NA | ., | <u> </u> | |
| | | 24 | | | - | += | |
| 1 | | 48 | | _1 | | | |

a - Dosage applied by technician indicated
NA - Not Applicable

Drecording error 8/9/8/8/

DERMAL SENSITIZATION STUDY IN GUINEA PIGS Sterile Test Test Group: RT No. 87 606 Vehicle 09 % salionaterial Let 1104 K 6410NA Positive Control Group NA Vehicle NA Animal No. 0399

Date Animal Received 7/0/81

Source Dean Daul Sex 6

Challenge Date 8/19/8

| | • | | | | Tech | Rec | |
|------------------------------|------------------------|-------------------------------------|----------|-------|------------|-------------|--------|
| Sensi- tizing Dose No. | Dose ⁴ (mi) | Obser- vation Period (Hrs) | Erythema | Edema | Technician | Recorded By | 1981 |
| | 0.4 | NA | NA · | MA | ٤٤ | ۶۹ | 7/22 |
| 1 | | 24 | 0 | 0 | Ne | ER. | |
| | 1.090 | 48. | 0 | 0 | IR | - J.C. | 7/24 |
| ` | 4 | NA. | NA | NA | MS | NDR | 7/29 |
| 2 | 1.0% | 24 | 0 | Q | 700 | MW | 7,(30) |
| | 1.0 10 | 48 | 0 | | 2 | 100 | 7131 |
| 7 | 0.4 | NA | NA | NA | R | R | 815 |
| 3 | | · 24 | | 0 | 1170 | 122J | 86 |
| | 1.0% | 48 | 0 | 0 | ΕŘ. | .56 | 817 |
| Challenge Dose | 0.4 | NA | NA. | NA | 50 | 50 | 8/19 |
| Dose | | 24 | 0 | 0 | 50 | de | 8/20 |
| | 1.090 | 48 | 0 | 0 | ۶۶ | du | 8/21 |
| | | NA. | NA | NA. | 17 | 41 | |
| | | 24 | | | | | |
| | | 48 | | 1 | | | |

a - Dosage applied by technician indicated

NA - Not Applicable

| | DERMAL S Test Group: | RT No. 871606 | IN GUINEA Sh Vehicle Q | <u>PIGS</u> trile Test 9 % saliopiete | Var | iso ft 175 <u>1104</u> K |
|---------|-----------------------|---------------|------------------------------|---|-----------|--|
| NA | | Group NA | | | 6410 |) – |
| Date Ar | nimal Received | 7/10/81 | | Date | Initiated | 7/22/81 |
| Source | Dean Day | Sex | | . Challe | nge Date | 8/19/81 |

| | | • | | | Tech | Rec | |
|------------------------------|-------------------|-------------------------------------|----------|-------|------------------|-------------|------|
| Sensi- tizing Dose No. | Dose ² | Obser- vation Period (Hrs) | Erythema | Edema | nician | Recorded By | 1981 |
| 1 | 0.4 | NA | NA | NA | દાર | EE | 7/22 |
| • | 1.090 | 24 48 · | CO | 0 | 412 12 | EP JK | 7/23 |
| 3 | 4 | NA | NA | NA | 20 | B | 7/29 |
| 5 | 1.0% | . 24 48 | - 0 | 5 | 100 | 28 | 7130 |
| 1 | 0.4 | NA | NA | NA | R | R | 815 |
| 3 | 1.0% | 24 . 48 | 0 | 0 | NDXI | NOV | 810 |
| Challenge Dose | | NA | NA. | NA. | | s R | 8/19 |
| Dose | 1.090 | 24 4 8 | O | 0 | ۶ و دو | des | 8/20 |
| | | - 114 | NA | NA | | | Ť, |
| | | 24 48 | | | | | |

a - Dosage applied by technician indicated . NA - Not Applicable

Date Animal Received 7/22

Source Doop Doul Sex 6 Challenge Date 8/9/8

| | • | | | | liech | Rec | |
|------------------------------|------------------------|-------------------------------------|----------|----------|--------------------------|-------------|------|
| Sensi- tizing Dose No. | Dose ^d (ml) | Obser- vation Period (Hrs) | Erythema | Edema | echnicien | Recorded By | 1981 |
| | 0.4 | . NA | KA | NA | ER | SE_ | 7/22 |
| | 1.090 | 24 48 | 0 | <u> </u> | MP | SP | 7123 |
| | 1.0 /6 | 49. | | 0 | 16 |)R | , , |
| 2. | 04 | na . | NA | NA | NON | RUN | 7/29 |
| æ . | 1.0% | 24 48 | | 0 | 150 | VDS | 1130 |
| 3 | 0.4 | n a | NA | NA. | R | R | 3/30 |
|) | 1.0% | - 24 48 | | 0 | M | NZO | 86 |
| Challenge. Dose | 0.4 | NA. | NA. | NA. | ξ <u>P</u> ε R | 5 <u>2</u> | 8 19 |
| Dose | 1.090 | 24 | 0 | 0 | 50 | da | 8/20 |
| | 1.0 10 | 4.8 | 0 | 0 | EP. | de | 8/21 |
| | | WA . | MA. | NA | , | <i>*</i> ′ | |
| | | 24 | | | | | |
| | | 48 | | | | | |

a - Dosage applied by technician indicated

| X Te | est Group: | RT No. 871606 | Sterile Sterile Vehicle 0.9 % s | Va Test alinevaterial Le | .risoft <u>t 1104</u> |
|-----------|----------------|---------------|---------------------------------------|--------------------------------|--------------------------|
| NA Po | sitive Control | Group A/A | VehicleNA | • • | 0403 |
| Date Anim | ual Received | 7/10/81 | · | Date Initiate | a <u>7 22</u> |
| Source 1 | Dean Day | Sex | | Challenge Date | 819 |

| | | | • | | Tech | Rec | |
|------------------------------|---------------------------|-------------------------------------|----------|-------|-----------|-------------|-------------|
| Sensi- tizing Dose No. | Dose ² (ml) | Obser- vation Period (Rrs) | Erythema | Edema | nician | Recorded by | 1981 |
| , | 0.4 | NA | NA | NA | ue | çe | 7/22 |
| • | 1.090 | 24 48 · | 8 | 0 | Me | ER. | 7/23 |
| 2 | 0.4 | NA | NA | NA | JR NOV | NO | 7/24 |
| ed · | 1.0% | 24 48 | 0 | 9 | 100 | I DO | 130 7/3/ |
| 2 | 0.4 | NA | NA | NA | R | 7 | 815 |
| .) | 1.0% | 24 48 | 0 | Co | ND0 | AIM) | 810 |
| Challenge. Dose | 0.4 | na | NA | NA. | 519 | ER_ | 8119 |
| Dose | 1.096 | 24 48 | 8 | /.0 | ER. | (CL) | 8/20 |
| | | HA | NA | NA | | ÷' | |
| | | 24 48 | . 143 | | | | |

a - Dosage applied by technician indicated NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Varisoft Test Group: RT No. 87/606 Vehicle 09% solioomaterial Let 1104 K

6410
NA Positive Control Group NA Vehicle NA Animal No. 0403

Date Animal Received 7/10/81

Source Dean Data Sex 6 Challenge Date 8/19/8

| | | | | | Tech | Rec | |
|------------------------------|---------------------------|-------------------------------------|-----------|--------|--------------------------|-------------|--------------|
| Sensi- tizing Dose No. | Dose ² (ml) | Obser- vation Period (Hrs) | Erythene. | Ed ene | Technician | Recorded By | 1981 |
| , | 0.4 | NA NA | NA | NA | ER. | ۶۵ | 7/22 |
| | 1.090 | 24 48 · | 0 | 00 | MAR | ER. | 7/24 |
| | 0.4 | NA | NA | NA | NIN | NX | 7/29 |
| 5 | 1.0% | 24 48 | 8 | 9 | N20 | IDR N | 7130 |
| 2 | 0.4 | N A | NA. | NA | R | 12 | 815 |
| 3 | 1.0% | · 24 48 | 0 | 00 | NOO | (D) | 80 |
| Challenge Dose | 0.4 | NA | NA | NA. | 50 | ER_ | 8 19 |
| Dose | 1.090 | 24 48 | 0 | 0 | 5 8 5 8 | da | 8/20 8/21 |
| | | *** | MA | NA | ., | ÷' | |
| | - | 24 48 | 0.00 | | | | |

a - Dosage applied by technician indicated

NA - Not Applicable

Drecording error 8/20/81 &

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Test Group: RT No. 871606 Vehicle 0996 SalionMaterial Lot 1104 Vehicle NA Animal No. 0404

Date Animal Received 7/10/81

Source Doop Date | Sex 3 Challenge Date 8/19/

| | | | | | liech Ch | Rec | _ |
|------------------------------|------------------------|-------------------------------------|------------------|-------|-------------|-------------|-------------|
| Sensi- tizing Dose No. | Dose ^d (ml) | Obser- vation Period (Hrs) | Eryth ens | Edena | echnisian | Recorded By | 1981 |
| , | 0.4 | NA | NA | NA | se. | SP. | 7122 |
| | 1.0% | 24 48 | 0 | 2 | MR | 50 JR | 7123 |
| | 7 0 | MA | NA | NA | NOV | 1170 | 7/29 |
| 3 | 1.0% | 24 48 | | 3 | M | 120 | 730 |
| 2 | 0.4 | NA | NA | NA | 13 | 7 | 815 |
| 3 | 1.0% | · 24 | Q | 0 | NOV) | NO | 86 817 |
| Challenge Dose | 0.4 | NA . | NA. | NA. | 88 | 58 | alia |
| Dose | 1.090 | 24 48 | 0 | 8 | 5 P. | de | 8/20 8/2 |
| | | NA. | MA | NA | • • | 419 | |
| | | 24 48 | | | • | | |

a - Dosage applied by technician indicated

Varisof+ 1

Test Group:

RT No. 871606 Vehicle 09% saliopaterial Lot 1104 K

6410-

NA Positive Control Group NA Vehicle NA Animal No. 0405

Date Animal Received

Date Initiated

Source Doan Day

Challenge Date 8 19 8

| | • | | | | rech | Rec | |
|------------------------------|---------------------------|-------------------------------------|----------|-------|------------|-------------|------|
| Sensi- tizing Dose No. | Dose ² (ml) | Obser- vation Period (Hrs) | Erythema | Edema | nician | Recorded By | 1981 |
| | 0.4 | na . | NA | NA | se. | 52 | 7/22 |
| | 1.0% | 24 48 · | 0 | 0 | M | se. | 1/23 |
| 2 | 0.4 | NA | NA | NA NA | NO | NJR | 7/29 |
| a | 1.0% | . 24 48 | 0 | 0 | 123 | 100 | 7/30 |
| 2 | 0.4 | NA | NA | MA | R | R | 815 |
| 3 | 1.0% | · 24 48 | 000 | 0 | N20 | 100 | 817 |
| Challenge Dose | 0.4 | NA. | NA. | NA | 50 | E E | 8/19 |
| Dose | 1.090 | 24 48 | <u> </u> | 0 | દ ે | des) | 8/20 |
| | | | | | | ÷ | 2/8/ |
| | | 24 | NA | NA | | , | 4, |
| | | 48 | | | | | |

a - Dosage applied by technician indicated

NA - Not Applicable

| | DERMAL S | ENSITIZATION STUDY | IN GUINEA P | <u>IGS</u> | الم عن م حد |
|----------|-------------|--------------------|-------------|--------------------------|-------------|
| Te | st Group: | RT No. 871606 | Vehicle 0.9 | Test To soline laterial | Lat 1104 |
| NA Pos | | Group | | | 6410- |
| | al Received | | | | ated 7/22 |
| Source I | Dean Day | Sex | | | 8 8 9 |

| | | | | | liec) | Rec | |
|------------------------------|-------------------------|-------------------------------------|----------|-------|------------|-------------|------|
| Sensi- tizing Dose No. | Dose ^a (ml). | Obser- vation Period (Hrs) | Erythema | Edema | Cechnician | Recorded By | 1981 |
| j | 0.4 | NA | , RA | NA | S.P. | SO | 7/22 |
| • | 1.090 | 24 48 · | 0 | 0 | 140 | 82 | 7123 |
| | 0.4 | | | 0 | 18 | | 7174 |
| 2 | | NA 24 | NA . | NA NA | NOW | NDO | 7/29 |
| | 1.0% | 48 | 0 | | 133 | Tw | 7/3/ |
| 2 | 0.4 | NA NA | NA NA | NA | | 7 | 815 |
| 3 | 1.0% | 24 | | 0 | 100 | KID | ষ্ঠি |
| Challes as | | 48 | | 0 | ER | ER | 817 |
| Challenge Dose | 0.4 | NA | NA | NA. | 50 | 80 | 8 19 |
| Dose | 1.090 | 24 | 0 | 0 | 50 | de | 8/20 |
| | 1.090 | 48 | 6 | 0 | . 88 | da | |
| | | NA. | MA | NA | | ¥' . | |
| | | 24 | | | | | |
| <u>_</u> | | 48 | | | | | |

a - Dosage applied by technician indicated NA - Not Applicable

Varisoft

Test Group:

RT No. 871606 Vehicle 09% salinguaterial Lot 1104

6410-

NA Positive Control Group NA Vehicle NA Animal No. 0407

Date Animal Received

Date Initiated 7/22

Source Dean Daw

Challenge Date 819

| | | , | | Tech | Rec | |
|-------------------|-------------------------------------|---|--|--|--|--|
| Dose ² | Obser- vation Period (Hrs) | Erythema | Edema | nician | orded By | 1981 |
| 0.4 | NA. | NA | na | EL | EE | 7122 |
| 1.090 | 24 48 | <u> </u> | 0 | WP | FP2 | 7123 |
| 0.4 | , NA | NA | NA | | Ι., | |
| 1.0% | . 24 | 0 | ð | 100 | 100 | 730 |
| | | | | 12 | R | 815 |
| | . 24 | | | NÃ | M | 8/10 |
| | | NA. | NA | | | 8/19 |
| | 24 | 0 | ් <i>ට</i> | ۶۶ | de | 8/20 |
| 1.0 10 | 48 | O | | <u> </u> | du | 8121 |
| | - NA | NA | NA | | <i>¥</i> ′ \ | |
| | | | | | | |
| | 1.090 (m1) | Dose ⁸ (ml) (Rrs) O.4 NA 1.0% 48 O.4 NA 1.0% 48 | Dose ² (ml) Period (Hrs) O.4 NA NA 1.090 48 0.4 0.4 0.4 0.4 0.4 0.4 0.4 0.4 0.4 0.4 | Dose Compare Compare | Dose Company Company | Obser-vaction Erythema Edema E |

a - Dosage applied by technician indicated

NA - Not Applicable

Dermal Sensitization In Guinea Pigs - Body Weights

Sterile

Varisoft 4

Test Group_ RT No. 871606 Vehicle 0.990 saline Test Compound Let 1104 K

NA Positive Control Group NA Vehicle NA

| | | | Animal | Number | • | | | Ť | |
|---------------|---------------|--------------|---------------|--------|---------------|-------|---------------|-----------------|-----------|
| 6410- 0427 | 6410- 0447 | 0409 0409 | 6410- 0411 | i | 6410- 0413 | 6410- | 6410- 0415 | Tech- nician | Da 198 |
| 359 | 357 | 362 | 401- | 340 | 2112 | 211 | | | |
| 415 | 3910 | | | | 342 | 361 | 360 | £ e | 7/2 |
| | | 409 | 477 | 418 | 397 | 416 | 420 | NDO | 7/2 |
| 457 | 454 | 462 | <i>5</i> 52 | 498 | 440 | 493 | 492 | | 8/5 |
| 506 | 505 | 520 | 604 | 562 | 429 | 540 | 564 | | 8/1 |
| 550 | 554 | <i>5</i> 80 | 663 | 621 | <i>5</i> 31 | 596 | 620 | | |
| | | | | | | 010 | 4 40 | ER | 8 10 |

| | | Animal Number | | |
|----------|---------------|-------------------------|-------------|----------|
| 1 | 6410- 0443 | | Tech- | Date 198 |
| 385 | 387 | Scale Used: K Tron 4809 | | |
| 445 | 459 | Scale Used: K-Trop 4009 | N=0 | 7/29 |
| 486 | 439 | Scale Used: K-Tron 4809 | NTO | 8/5 |
| 566 | 592 | Scale Used: KTRON 4809 | Dh | |
| 633 | 653 | Scale Used: KiTron 4809 | ER | 8/19 |
| | _ | Scale Used: | - UZ | 0/14 |

Dermal Sensitization in Guinea Pigs - Daily Observations Varisoft 475

Sterile
Test Group RT No. 871606 Vehicle 9% saline Test Compound Lot 1104 K

Positive Control Group NA Vehicle NA Room No. 2

NA

 \mathcal{Q} Sax Animal Number 6410-6410-6410-6410-6410-6410-6410-6410-Tech-0427 0447 0409 0411 nician Date 0412 0413 0414 0415 198 N 7/22 Ν Ν N N N 93 \mathcal{N} Ν \wedge Λ Ν M 7/23 Ν ER N Ν Ν \mathcal{N}_{\cdot} N 7124 Ν Ν N N 7/25 N ノ N 1 7/26 N 2/27 N N N 11 N · N N VCU. 1/29 N N N 1.1 7/29 N NCW N N N N N N N 7/30 S Ы 2 7/31 8/1 N N 2 N N N N N. 2 N S 8/2 2 mo 2 N N 8/3 N N 2 N Δ N dhe Λ NJ N $\cdot \mathcal{N}$ N N N N N 25 N JP ~ 8/6 N NTO N 8/7 N N N N N N ER 8/8 V 1

N - No Visible Abnormalities

| | Dermal | Sensitiz | ation in | Guines P | igs - Da | ily Obser | Vations | | |
|---------------|------------|------------|--------------|-------------|----------------|-----------|----------|---------|-------------|
| \boxtimes | Test Group | RT No. 9 | 271/201 | W-1-1 | Sterile | | | Varisof | + 475 |
| | Test Group | , wr 40. | 211606 | Aeurcle | <u>0990 so</u> | lineTest | Compound | 10+ 110 | <u>4 K</u> |
| NA | Positive C | control Gr | oab <u>\</u> | 4 ve | hicle / | V.A | Room No. | 2 | |
| | Sex 9 | 2 | | | | | | | |
| | | An | imal Numb | er | | | | _ | |
| 6410 | - 6410- | | | | | | | | |
| | 0443 | | | | | ı | | Tech- | |
| | 0793 | | | | | | | nicien | Date |
| | + | | | | | | | | 1981 |
| N | I N | | | | | | | EP | 7/22 |
| N | N | | | | | | | ER | 7/a3 |
| N | N | | | | | | | /R | 7/24 |
| N | N | | | | | | | JP | 7/25 |
| N | N | | | | | | | | |
| 1 | N | | | | | | | 18 | |
| N | N | | | - | | | | JR | 7/27 |
| N | N | | | | | | | NO | 7/28 |
| N | N | | · | | | | | PCV | 7/29 |
| | | | | | | | | NJX | 7/30 |
| N | N | | · | | | | | DR | 7/31 |
| - 2 | N | | | | $\overline{}$ | | | det | 8/1 |
| 2 | 2 | | | | | 1 | | TYP | 8/2 |
| \sim | \ <u>\</u> | | | | | | | che | 8/3 |
| N | N | | | | | | | cs | 1/4 |
| \mathcal{N} | N | | | | | | | TP | 8K |
| \mathcal{N} | N- | | | | | | 1 | | 8/6 |
| N | N | | | | | | | 1 | 8/7 |
| N | N | | | | | | | ER JY | 8/8 |
| | | | | | | | <u> </u> | ノイ | 0/8 |

N - No Visible Abnormalities

Dermal Sensitization in Guinea Pigs - Daily Observations

Varisoft 475 Test Group RT No. 871606 Vehicle 9% saline Test Compound Lot 1104 K NA Positive Control Group NA Vehicle NA Room No. 2 Sex 9 Animal Number 6410-6410-6410-6410- 6410-6410-6410-6410-Tech-0427 0447 0409 0411 0412 nician 0413 Date 0414 0415 1981 8/9 TP IJ N N 8/10 da 8/1 N در 81 N N 8/13 N N N ER 8/14 8/15 Ν 8/6 da. 8/17 N 8/18 N N N N 5R 8/19 N N N N N ${\mathcal N}$ N 8/20 dov N N N \mathcal{W} N S W 8/21 do

N - No Visible Abnormalities

| | Derma | l Sensiti: | zation in | Guines | Pigs - Da | ily Obse | Evatione | | | |
|--------------|-----------------------------|------------|----------------------------|------------|-----------|--|----------|-----------------|--------|--|
| \mathbf{X} | Test Grou | P RT No. | 871606 | Vehtc1 | Sterile | 1. | | Variso: | ft 475 | |
| VA | Posteine i | 3 | <u> </u> | | <u> </u> | linerest | Compound | 1 10+ 110 | 4 K | |
| | Positive (| onerso⊺ Cr | Lonb \(\bullet \rangle \) | <u>A</u> v | hicle _ | VA | Room No. | _2_ | | |
| | | | | | | | | | | |
| 0410 | Animal Number 6410 - 6410 - | | | | | | | | | |
| | 0443 | | | | | | | Tech- nician | Date | |
| | | | | | | | | | 1981 | |
| N N | 1 n | | | | | | | | | |
| N | N | | | | | | | JP | 8/9 | |
| 1 | N | | | <u> </u> | | | | new _ | 8/10 | |
| | | | - | | | | | 12 | 8/11 | |
| N | N | | - | , | | | | Ne | 8/15 | |
| | | | | | | | | ER | 8/13 | |
| <u>u</u> | N | | | | | | | Q) | 8/14 | |
| - ,- | N | | | - | | | | De | 8h5 | |
| N. | N | | | | | | | JP. | 8/16 | |
| N | N | | | • | | | | da | 8/17 | |
| N | N | | | | | | | | | |
| 1/ | N | | | | 1 | | | Se | 8/18 | |
| Ν | N | | · | | 1 | | | ER | 8/19 | |
| N | N | | | · | | \ | | da | 8/20 | |
| | | | | · | | | | da | 8/2/ | |
| | | | | | | | | | | |
| | | | | | | | | | | |
| | | | - | | | | | | | |
| | | | | | | | | | | |
| | | | | | | | | | | |

N - No Visible Abnormalities

| DERMAL S Test Group: | RT No. 871606 | IN GUINEA PIGS Sterile Vehicle 09 % | Va. Test Salinevaterial Loi | risoft 1 <u>r 1104</u> K |
|-----------------------|---------------|-------------------------------------|-----------------------------------|-----------------------------|
| NA Positive Control | | | 641 | 0- |
| Date Animal Received | 7/10/81 | _ | Date Initiated | 7/22/ |
| Source Dean Day | Sex P | | Challenge Date | 8/19/8 |

| | • | | | | Tect | Rec | L, |
|------------------------------|---------------------------|-------------------------------------|----------|-------|--------------|-------------|--------------|
| Sensi- tizing Dose No. | Dose ² (ml) | Obser- vation Period (Hrs) | Erytheme | Edene | rechnicien . | Recorded by | 1981 |
| 1 | 0.4 | na | KA | NA | ۶۶ | ٤٤ | 7/22 |
| | 1.0% | 24 48 | 0 | CO | JR | 7.6 E.6 | 7/24 |
| | 0.4 | NA | NA | NA | NOR | NDO | 7/29 |
| a | 1.0% | . 24 48 | 0 | 0 | NTO | M | 7130 |
| (| 0.4 | NA | NA | NA | R | R | 815 |
| 3 | 1.0% | · 24 | 0 | 0 | NOO ER | 1177) ER | 811 |
| Challenge Dose | 0.4 | NA | NA. | NA. | 50 | 50 | 8119 |
| Dose | 1.096 | 24 4 8 | 0 | 0 | E P | da | 8/20 8/21 |
| | | -XA | NA | NA | 1 | - | |
| | | 24 | WA | , ta | , | | |
| | | 48 | | | | | |

a - Dosage applied by technician indicated
 NA - Not Applicable

| DERMAL | SENSITIZATION STUDY | IN GUINEA PIGS | Va | -i < ~£+ ' |
|------------------------|---------------------|-----------------|--------------------------|------------|
| Test Group: | RT No. 871606 | Vehicle 0.9% sa | Test linematerial Loi | - 1104 K |
| NA Positive Contro | l Group | Vehicle NA | 6410 Animal No. | _ |
| Date Animal Received _ | 7/10/81 | _ | Date Initiated | 7/22/ |
| Source Dean Day | Sex <u> </u> | | Challenge Date | 8/19/ |

| | .₩ | | | | | | |
|------------------------------|------------------------|-------------------------------------|----------|-------|-------------|-------------|--------------|
| Sensi- tizing Dose No. | Dose ⁴ (ml) | Obser- vation Period (Hrs) | Erythema | Edena | Technician | Recorded By | 1981 |
| , | 0.4 | NA. | NA | NA | EP. | ٤٤ | 7/22 |
| | 1.0% | 24 48 · | 0 | 8 | MR | EP. | 7123 |
| 2 | 04 | NA | NA | NA | NOR | NOD | 7/29 |
| 5 | 1.0% | 24 48 | 0 | 0 | 100 | ija | 7130 |
| 2 | 0.4 | NA | NA NA | NA | N | R | 8/5 |
| 3 | 1.0% | · 24 48 | 000 | 0 | NX | rom ES | 817 |
| Challenge Dose | 0.4 | NA | NA | NA | ٤٥ | ٤٤ | 8)19 |
| Dose | 1.090 | 24 48 | 8 | 0 | EP. | de | 8/20 8/21 |
| | | *** | MA | NA | ., | <i>4</i> | |
| · | | 24 48 | | | | | |

a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Varisof+ 47

Test Group:

RT No. 871606 Vehicle 09% salinevaterial Lot 1104 K

6410-

NA Positive Control Group NA Vehicle NA Animal No. 0409

Date Animal Received 7/10/81

Date Initiated 7/22/8

Source Dean Day Sex 7

Challenge Date 8/19/8/

| | • | | | | Tech | Reco | |
|------------------------------|------------------------|-------------------------------------|----------|--------|------------|-------------|------|
| Sensi- tizing Dose No. | Dose ⁴ (ml) | Obser- vation Period (Hrs) | Erythema | Edena | Technician | Recorded By | 1981 |
| 1 | 0.4 | NA | NA | NA | 5E | 58 | 7/22 |
| | 1.090 | 24 48 | 00 | 0 | MR. | EQ. | 7/24 |
| (| 0.4 | NA | NA | NA | NOV | NJA | 7/29 |
| | 1.0% | . 24 48 | - 0 | 0 | NOO | MA | 7,30 |
| 1 | 0.4 | NA | NA | NA | R | R | 8/5 |
| 3 | 1.0% | · 24 48 | Co | 0 . | NOO ER | NM ER | 26 |
| Challenge | 0.4 | NA | NA. | NA. | SP | ER_ | 8/19 |
| Challenge Dose | 1.090 | 24 48 | 0.5 | 0 | 5 P | da | |
| | | *A | NA | NA | , | ÷1 | 4.0 |
| | | 24 | NA. | , turk | | | |
| | | 48 | | | | | |

a - Dosage applied by technician indicated

NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Varisof+1

RT No. 871606 Vehicle 09 % salionaterial Lot 1104 K Test Group: 6410-

NA Positive Control Group NA Vehicle NA Animal No. 0411

Date Animal Received Date Initiated 7/22/8

Source Dean Day Challenge Date 8/19/81

| | • | | | | <u> </u> | | |
|------------------------------|---------------------------|-------------------------------------|----------|-------|------------|-------------|-------------|
| Sensi- tizing Dose No. | Dose ⁴ (ml) | Obser- vation Period (Hrs) | Erythems | Edeme | Technician | Recorded By | 1981 |
| , | 0.4 | NA NA | KA . | NA | ER | ٤٤ | 7/22 |
| | 1.0% | 24 48 · | 0 | 8 | we | CE: | 7 23 |
| 2 | 0.4 | na | NA. | NA | NON | NOD | 7/29 |
| - | 1.0% | 24 48 | 2 | 0 | NÃO | MON | 7/3/ |
| 3 | 0.4 | NA | NA | NA | R | 7 | 815 |
| | 1.0% | · 24 | 0 | 0 | NOW | NTO | |
| Challenge Dose | 0.4 | NA | NA. | NA. | EQ. | 52 52 | عام اه |
| Dose | 1.090 | 24 48 | 0.5 | 0 | 82 | de | 8/20 |
| | | MA | NA NA | na | ee | AQ) | 8/2/ |
| | | 24 48 | | | | | |

a - Dosage applied by technician indicated

| | RT No. 871606 | IN GUINEA PIGS Sterile Vehicle 09% S | Var Test Uncaterial Lot | 150f+ 1 1104 K |
|----------------------|-----------------|--------------------------------------|-------------------------------|-------------------|
| | Group <u>NA</u> | | 6410 |) • |
| Date Animal Received | 7/10/81 | _ | Date Initiated | 7/22/ |
| Source Dean David | Sex P | | Challenge Date | aliala |

| | • | | | | Hech | Reco | |
|------------------------------|---------------------------|-------------------------------------|----------|-------|------------|-------------|------------|
| Sensi- tizing Dose No. | Dose ² (ml) | Obser- vation Period (Hrs) | Erythema | Edema | Technician | Recorded By | 1981 |
| 1 | 0.4 | NA | NA | NA | جو | 52 | 7/22 |
| | 1.0% | 24 48 | 0 | 00 | J.K. | ER. | 7124 |
| | 94 | NA | NA | NA | NOR | WD | 7/29 |
| ھ | 1.0% | . 24 | 2 | 8 | NOO | NTO N | 7/30 |
| (| 0.4 | NA | NA | NA | R | 7 | 815 |
| 3 | 1.0% | 24 | Co | 9 | YIM EE | NOV ER | 817 817 |
| Challenge Dose | 0.4 | NA | NA | NA. | ٤٥ | ER | 8/19 |
| Dose | 1.096 | 24 | 0 | 0 | SP SP | du | 8/20 |
| · | | NA. | MA | NA. | - 17 | 4' | |
| | | 24 | 0.45 | | | | |

a - Dosage applied by technician indicated
 NA - Not Applicable

| Test | DERMAL Group: | RT No. 871 | | Sterile Sterile Le 0.9 % sa | Test linewaterial | Varisoft 175 Lot 1104 K |
|------------------------------|-------------------|----------------------------|------------|-----------------------------------|----------------------|----------------------------|
| NA Pos | itive Contro | l Group | Vehic | ie <u>NA</u> | Animal | No. 0413 |
| | Received | 7 10 8 | <u>\$1</u> | | | iaced 7/22/81 Date 8/19/81 |
| | | • | | | Tec Rec | |
| Sensi- tizing Dose No. | Dose ⁴ | Obser- vation Period | Erythema | Ed ema | orded By | |

| Sensi- tizing Dose No. | Dose ^a (ml) | Obser- vation Period (Hrs) | Erythema | Edema | ician . | orded by | 1981 |
|------------------------------|---------------------------|-------------------------------------|----------|-------|------------|----------|------|
| | 0.4 | NA | RA | NA | EP | ER | 7/22 |
| | 1.090 | 24 48 · | 2 | 8 |)R | - EE | 7/24 |
| 7 | 0.4 | NA | NA | NA | NUR | VX | 7/29 |
| | 1.0% | . 24 | 0 | 0 | MO | 100 | 7130 |
| 2 | 0.4 | NA | NA | NA | R | R | 815 |
| 3 | 1.0% | 24 48 · | ·O | 0 | NOX) FR | NTO | |
| Challenge Dose | 0.4 | na | NA | NA · | 8.2 | ٤٤ | 8/19 |
| | 1.090 | 24 48 | 0 | 0 | se. | de | 8/21 |
| | | *** | NA | NA | | | |
| | | 2 4 48 | | | | | |

a - Dosage applied by technician indicated NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Varisof+175

Test Group: RT No. 871606 Vehicle 09% soling aterial Let 1104 K
6410
NA Positive Control Group NA Vehicle NA Animal No. 0414

Date Animal Received 7 10 81

Date Initiated 7 2281

Source Doop Day Sex 4 Challenge Date 8 1981

| | .• | | | | Tech | Rec | ٩ |
|------------------------------|---------------------------|-------------------------------------|----------|----------|--------|--------------------|------|
| Sensi- tizing Dose No. | Dose ⁴ (ml) | Obser- vation Period (Rrs) | Erythema | Edema | nician | Recorded by | 1981 |
| • | 0.4 | na | NA | NA | ER | ٤٥ | 7 22 |
| l l | | 24 | Q | 0 | Me | ER | 7123 |
| | 1.090 | 48. | 0 | <u> </u> |) R_ | 118 | 7)24 |
| 2 | 04 | HA | NA | NA | NUR | MAX | 7/29 |
| | 1.0% | . 24 . | - 0 | Q_ | NTD | 1 in | 7130 |
| | | 48 | | | 1.17 | ++>= | 7131 |
| | 0.4 | NA | NA | NA | R | R | 815 |
| 3 | | 24 | | 0 | 720 | | 86 |
| | 1.0% | 48 | | 0 | ٤٤ | ER | 817 |
| Challenge | 0.4 | NA | NA | NA | 50 | ٤٤ | ही।१ |
| Challenge Dose | 1.090 | 24 | 0 | 0 | S.E. | | 8/70 |
| | | 48 | 0 | | 56 | da | 8/21 |
| | | *** | NA | NA | | - - 2 - | |
| | | 24 | | | | | |
| | 1 t | 48 | | | | | |

a - Dosage applied by technician indicated

NA - Not Applicable

|] Posi | Group: | RT No. 871 1 Group | STUDY IN GUIN LaO (a) Vehicle A Vehic | sterile 0.990 sa | Ani | erial mal No Initi | Lot 11 6410 - | _ |
|--------|---------------------------|-------------------------------------|---|---------------------|--------------------|--------------------------|------------------|---|
| ii- | Dose ⁴ (ml) | Obser- vation Period (Hrs) | Erythema | Edema | Technician | Recorded By | 1981 | |
| | 0.4 | ₩ A 24 48 | NA CO | NA 00 | 62 11118 114 | E & | 7/22 | |
| 3 | 0.4 | NA 24 48 | NA C | NA O | | 100 | 7/29 | |
| 3 | 0.4 | NA 24 48 | NA O | NA O | 77 1000 ER | 300 | 816 | |
|)03e | 1 | NA 24 | NA D | NA O | ER. | 52 de) | 8/19 8/20 | |

NA

NA

24

⁻ Dosage applied by technician indicated - Not Applicable

Test Group: RT No. 871606 Vehicle 09% Saliomaterial Lot 1104 K NA Positive Control Group NA Vehicle NA Animal No. 0416

Date Animal Received 7/10/81 Date Initiated 7/22/8

Source Doop Dayl Sex 4 Challenge Date 8/19/81

| | | | | | Tech | Reco | Ē. |
|------------------------------|---------------------------|-------------------------------------|----------|-------|-----------|-------------|------|
| Sensi- tizing Dose No. | Dose ⁴ (ml) | Obser- vation Period (Hrs) | Erythema | Edema | mician | Recorded By | 1981 |
| • | 0.4 | na. | na . | NA | يو | وو | 7/22 |
| 1 | 1.0% | 24 48 · | 0 | 0 | MP | ER. | 7/23 |
| | 0.4 | NA | NA | AM | NOO | NON | 7/29 |
| 5 | 1.0% | 24 | 0 | 9 | MODE | 100 | 7/30 |
| | 0 4 | NA | NA . | NA _ | R | R | 8/5 |
| 3 | 1.0% | 24 | 0 | Q | KIN | WXX ER | 810 |
| Challenge | | NA. | NA. | NA | ٤٤ | Ε 2 | 8/19 |
| Challenge Dose | 1.090 | 24 | 8 | 8 | ER. FR | dev | |
| | | *** | NA | NA | | - 21 5 | |
| | | 24 | | | | | |
| 1 | | 48 | | | <u> </u> | 1 | |

a - Dosage applied by technician indicated

NA - Not Applicable

| | _ <u>DERMAL_S</u> | ensitization rt no. 8711 | STUDY | in cuinea Ste | PIGS | Test | Vari | 50f+ 1' |
|-----------|-------------------|-----------------------------|----------|------------------|------|-------------|--------------|----------|
| | est Group: | RT No. SIII | | | | | 6410 | - |
| NA Po | ositive Control | Group | <u> </u> | Vehicle | NA | Animal N | lo. <u> </u> | <u> </u> |
| Date Anim | mal Received | 71.0181 | | _ | | Date Initi | | |
| Sau-20 | Dean Day |) Sex | 9 | | • | Challenge D | ate | 8/19/8 |

| | • | | | | Tech | Reco | = |
|------------------------------|------------------------|-------------------------------------|----------|-------|--------|-------------|----------|
| Sensi- tizing Dose No. | Dose ⁴ (mi) | Obser- vation Period (Hrs) | Erythema | Edema | niciau | Recorded by | 198 |
| | 0.4 | NA | NA | NA | · ER | ER | 7/22 |
| ı | | 24 | 0 | | WE | 50 | 7/23 |
| | 1.0% | 48 | 0 | 0 | JK | 112 | 7/24 |
| ~ | 0.4 | NA | NA | NA | MXX | WY | 7/20 |
| 2 | 1.0% | 24 48 | 2 | 19 | 150 | Ma | 7/31 |
| <u> </u> | 0.4 | NA. | NA | RA | 3 | R | 815 |
| 3 | | 24 | Q | | NDO | NOO | 817 |
| | 1.0% | 48 | 0 | 0 | ٤٤ | 1 1 | 1011 |
| Challenge Dose | 0.4 | NA | NA | NA | se | ۶۶ | 8/19 |
| Dose | 100 | 24 | ٥ | 0 | 58 | | 8/20 |
| | 1.090 | 48 | 0 | | Eb | del | 8/91 |
| | | NA- | MA | NA | | | |
| | | 24 | | | 4 | <u> </u> | <u> </u> |
| | | 48 | | | | | |

a - Dosage applied by technician indicated NA - Not Applicable .

| | ^ | Derma] | L Sensi | tization | ı In G | Suinea Pig | s - Body | Weight | :s | | |
|---|--------------------|--------|---------|---------------|--------|------------|----------|----------------|----------|----------------------|-----|
| V | O Naive | 2 | | △ = 1. | _ | Sto | rile | | | Varisoft Lot 1104 | 475 |
| | Test Gr | coup E | RI No. | 8.111 | ۷ مان | Wehicle O | % salin | <u>n</u> eTest | Compound | Lot 1104 | K_ |
| | Positiv | | | | | | e NA | | | | |

| | | | Animal | Number | | | Ī | |
|---------------|---------------------|-------------------------|--------------------|--------|---|--|-----------------|--------------|
| 6410- 0378 | 6410 - 0390 3 | 6410- 0- 0- 0- | 6410- 0408 9 | | | | Tech- nician | 1981 Date |
| | 366 | 324 | 326 | | | | ೯೯ | 7/22 |
| 435 | 446 | 401 | 403 | | | | 100 | 7/29 |
| 504 | 518 | 463 | 462 | | | | JR | 8/5 |
| 580 | 561 | 506 | 525 | | _ | | DR | 8/13 |
| 628 | 607 | 559 | 579 | | | | ER. | 8 19 |
| | | | • | | | | | |

| | Animal Number | <u> </u> | |
|---|--------------------------|----------|--------------|
| | | Tech- | 1981 Date |
| | Scale Used: K. Tron 4809 | ER. | تراءء |
| | Scale Used: K-Tron 4809 | - PD | 7/29 |
| | Scale Used: K-Tron 4809 | 18 | 9/5 |
| | Scale Used: K TRON 4809 | De | 8/12 |
| | Scale Used: KiTron 4809 | ER | 8/19 |
| 7 | -Scale Used: | | |

NA - Not Applicable

D form change 7/21/81 ER

| 1 | Dermal Sen | - sitization | in Guine | a Pigs - 1 | Daily Obser | Vations | Varisoft | ムった |
|---------|------------------------|-----------------|----------|------------|-------------|----------|----------------------|----------|
| Naiv | ∕ € Group RT | No. 87160 |)(ø Vehi | sterile | soline Test | Compound | Varisoft Lot 1104 | 713 K |
| NA Posi | tive Contr | ol Group _ | NA | Vehicle. | NA | Room No. | 2 | |
| | | Animal N | lumber | | | , | 7 | |

| | | An | imal Numb | er | | • |]. | |
|---------------|--------------------|--------------------|-----------|----|--|---|-----------------|--------------|
| . C. 8760 | 6410- 0380 8 | 6410- 0410 9 | 0408 P | | | | Tech- nician | Date 1981 |
| N | N | N | N | | | | ER | 7/22 |
| N | N | N | N | | | | ER | 7/23 |
| N | N | N | N | | | | K | 7/24 |
| W | N | N. | N | | | | R | 7/25 |
| N | N | N | N. | | | | JK | 7/26 |
| | N | W | N | | | | JP | ר גור |
| | Λ/ | Λ/ | . // | | | | 1/20 | 7/28 |
| | Λ/ | ^/ | \sim | | | | 1/20 | 7/29 |
| N | N | N | N | | | | NOX | 7/30 |
| 7 | ~ | N | N | | | | Sh | 7/31 |
| 2 | 2 | N | N | | | | 770 | 8/1 |
| _ N_ | 2 | 2 | 2 | | | | der | 8/2 |
| 2 | 2 | 2 | 2 | | | | de | 8/3 |
| N | N | N | N | | | | CS | 8/4 |
| \mathcal{N} | N | N | N | | | | R | 815 |
| // | N | √ - | -N | | | | NOO | 86 |
| N | N | N | N | | | | æ | 8/1 |
| 1/ | N | N | 11 | | | | F | 3/0 |

N - No Visible Abnormalities

NA - Not Applicable

Oform change 7/21/81 ER

| | est Group | RT No. | 371606 oupNA | Vehicle | 990 soli | Delest Co | perpodence | 110 خم | + 475 <u>+ K</u> |
|---------------|---------------|--------|-----------------|---------|----------|-----------|------------|-----------------|---------------------|
| 6410 - | | 6410- | imal Numb | er \ | | | | | |
| 0378 | 0380 | | 0408 2 | | · | | | Tech- nician | Date 1981 |
| N | N | N | N | | | | | R | 8/9 |
| N | N | N | N | | | | | da | 8/10 |
| N | N | N | i | \ | | | | JR | 8//1 |
| 7 | 7 | 7 | N | | | | | De | حالع |
| N | N | Ν | Ν. | | | | | ER | 8/13. |
| N | , N | N | N | | | · | | ولم | 8/14 |
| ~ | 2 | N | . N | · | . \ | | , | Da | 8/15 |
| \mathcal{N} | \mathcal{N} | N | N | | | | | JK | 8/16 |
| N N | N | ν | N | | | | • | da | 8/17 |
| N | 7 | N | N | | | | | De | 8/18 |
| N | N | N | N | | | | <i>i</i> . | ER | 8/19 |
| N | N | Ν. | λ | | | | | del | 8/20 |
| N | N | Ŋ | \mathcal{N} | | | | | dw | 8/21 |
| | | | | | | | | | |

N - No Visible Abnormalities

NA - Not Applicable.

Oform change 7/21/81 ER

Varisoft 475 sterile Test Varisott 4
RT No. 871606 Vehicle 0990 Saline Material Lot 1104

7/10/81 Date Animal Received Source Dean Daul

Date Initiated 7/22/81 Challenge Date _

| | | | | | a | | |
|------------|-------------------|-------------------------------------|--------------|-------|----------------------|-------------|----------|
| | • | | , | | Teclu | Rece | <u> </u> |
| Animal No. | Dose ² | Obser- vation Period (Hrs) | Erythema | Edema | Technician | Recorded By | 1981 |
| 0378 | 0.4 | NA | NA | NA | ER | ER | । । |
| 3 | 1.0% | 24 48 | 0,5 | 0 | <u> </u> | de | 8/20 |
| 0380 | 0.4 | NA | NA | NA | £Ω | ER | 8/19 |
| 3 | 1.0% | 24 48 | 0 | 0 | E 2 | de de | 8/20 |
| 0410 | 0.4 | NA. | NA | · NA | ٤٥ | 1 88 | ١٩١٩ |
| 2 | 1.0% | 24 48 |)) | 0 | FQ | des | 8/20 |
| 0408 | 0.4 | NA | RA | NA | SP | ا دو | 8/19 |
| 9 | 1.0% | 24 48 | O | 0 | । ६ <u>८</u> । ६८ | de | 8/20 |
| | | 114 | XA. | NA | | 1 | |
| | | 24 48 | | | | | |

a - Dosage applied by technician indicated

NA - Not Applicable

Naive Group:

Oform change 7/21/81 ER

| | Dermal | Sensitiz | ation in | Guinea Pi | gs - Dail | y Observa | tions V | arisc ít t | 175: Lot |
|---------------|-----------|-----------|-----------|------------------|-------------------|-------------------|-------------|-----------------------|-------------------------------|
| X T | est Group | RT No. 8 | 371605 | Ste Vehicle (| rile 2990 sali | og Test Co | Vocuocom | risa () Um | 175: Lot <u>5: Lot</u> 195 |
| NA Po | adadaa C | 1 C | 371607 | and | | | • | 2 | <u> </u> |
| EA P | DRICINE C | outlot Gr | orb | ven | TCIE | NA RC | OT NO. | <u> </u> | |
| | | An | imal Numb | er - | | | | 7 | |
| 6410- | 6410- | | 6410- | | | | | | |
| | | | 0424 | | | | | Tech- nician | Date |
| | | 911 | 127 | 0 /25 | | | <u> </u> | | 1981 |
| N | N | N | N | N | | | | ER. | 8/26 |
| N | N | Ν | N | N | | | | ER | 8/27 |
| \mathcal{N} | N | N | N | N | | | | Je | 8128 |
| | | | | | | | | | |
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| | | • | | | | | | | |
| | | | | | | | | | |

N - No Visible Abnormalities

NA - Not Applicable

NA

| | B | | | , | | _ | |
|-----------------------------|---------------------------|-------------------------------------|------------------|----------------------------------|-----------------------|----------------|--------------------|
| | DERMAL | SENSITIZATION | STUDY IN GUI | NEA PIGS | | A Vai | risoft 4 |
| Test | t Group: | RT No. <u>(A) 87</u> (B) 87 | Vehicl | erile • 0.99 ₀ sal | Tes <u>in</u> Mat | t 😥 (erial | varisoff Lot 19 |
| Pos: | | | A Vehic | | | imel ! | |
| te Animal | l Received | 7/10/21 | | | | | iated <u>E</u> |
| rce D | zan Da | Sex | <u> </u> | • | Chall | enge 1 | Date 8 |
| | • | | | | = | - | - |
| | | | | , _ | ech | 529 | |
| nimal initial izing ica No. | (ml) Dose ^a | Obser- vation Period (Hrs) | Eryth ema | Edema | rechnician rechnician | Recorded By | 1981 |
| 410- | 0.4 | NA | NA. | NA | ε e . | 122 | 8126 |
| 402 (A | <u> </u> | 24 | 0 | 0 | 60 | 60 | 827 |
| 7 w 6 | 1.0% | 48 · · | 0 . | 0 | NOO | ER | 8/18 |
| 410- | 0.4 | NA | NA. | NA | 60 | 50 | 8126 |
| 402 ₆ | 100 | 24 | 0 | 0 | ee. | 50 | 8 27 |
| | 1.0% | 48 | 0 | | 100 | EQ. | 8/38 |
| | | NA. | NA | NA . | | | |
| | | 24 | | | | | |
| | | 48 | | | <u> </u> | - | + |
| | | NA | NA. | NA | | | |
| | | 24 | | | 1 | 1 | |

NA

48

NA 24 48

a - Dosage applied by technician indicated NA - Not Applicable

(1) form change 8/25/81 ER

| | DERMAL | SENSITIZATION STUDY | IN GUINEA P | IGS | @ Variso | + 475, |
|--------|------------------|---|-------------|--------|--------------|------------------|
| ₩ | Test Group: | SENSITIZATION STUDY A 871605 RT No. B 871607 | Vehicle C. | tile I | est g varis | 1138 K 195-13 |
| MA | Positive Contro | 1 Group <u>NA</u> | Vehicle | NA - | Arisel No. | • |
| | nimal Received _ | · · | | Da | te Initiated | <u> </u> |
| Source | DeanDau | () Sex 3 | | - Cha | llenge Date | 8/26/8 |
| | • | · | | | | |

| | • | • | | | Tech | Rec | |
|--------------------------------------|---------------------------|-------------------------------------|----------|---------|------------|-------------|-------------|
| Animal Sensi Lising Bose No. No. | (ml) Dose ² | Obser- vation Period (Hrs) | Erythema | Edema | rechnician | Recorded By | 1921 |
| 0110- | 0.4 | NA | NA | NA | ۶ و | EP. | 8/26 |
| 0393 | | 24 | 0 | O | ER. | FR. | Blan |
| 6 | 1.0% | 48 | C | | 700 | 56 | 8/38 |
| ا - 10 بدی | 0.4 | NA | NA | NA | جع | ER | 8/26 |
| 03936 | 100 | 24 | 0 | | ee. | ER | 8,51 |
| | 1.6% | 48 | 0 | 0 | KOK | 86 | 8 28 |
| | | NA. | NA | NA. | | | |
| | | 24 | | | | | |
| | | 48 | \$ | | | | |
| 6410- | 0.4 | NA | NA | NA | ER. | 99 | 8126 |
| 0394A | 17.01 | 24 | 0 | 0 | 66 | ER | 8 27 |
| | 1.690 | 48 | 0 | | NW | 66 | 8 28 |
| 6410- | 0.4 | NA | AM | NA | 22 | ER | 8/26 |
| 03946 | 1.690 | 24 | 0 | 0 | 50 | ER | 8/27 |
| | 1 1 C 10 [| 48 | | | M | 66 | 8128 |

a - Dosage applied by technician indicated NA - Not Applicable

1) form change 8/25/81 ER.

| | D | | | | | | |
|-------------|-------------------|-----------|--------------|------------------------|-----------------|--------------|------------|
| | DERMAL | | STUDY IN GUI | NEA PIGS | | @Var | isoff 47 |
| - | | A 87. | 1605 | iterile • 0.940 sal | Tes | tB) Va | irisoft, |
| Test. | Group: | RT No. | Venici | e 0.440 sal | ICZ Mat | erial | 19. |
| ` | | B 87 | 1607 | | | | |
| A Posi | tive Contro | 1 Group A | VA Vehic | le NA | | imel 1 | io. |
| A | | | <u> </u> | • | | | |
| | | 7/ /01 | | | . | • • • | |
| te Animal | Received _ | 7/10181 | 0x 9 | | Date C-Chall | TOTE | raced |
| | 22 | / Sex | (1) X (2) | . 7 | a-Chall | enge | Date S |
| 1 CE 1 1/ | (11) - 1-1111 | | | ^ | | | |
| | | | • | | | | |
| | • | | | | | , | T |
| | | | | | 66 | Re | L |
| () a " 1 | \ | | • • | | | Recorded | Date |
| Animal | (m1) | Obser- | · | | <u> </u> | de | (r) |
| ising | Dose ² | vation | Erythema | Edema | | | 1 |
| ose No. | { } | Period | | | 1. | By | 1,00, |
| من | | (Hrs) | | | | | 1981 |
| 10. 410- | 0.4 | na | NA | NA | قع ا | ER | 8/26 |
| מורווי | | 24 | 0 | 0 | ER. | 56 | 827 |
| 1424A | 1.0% | 48. | 0 | 0 | NIN | 58 | 8 28 |
| 2410- | T | | | 1 | |) | |
| | 0.4 | NA. | NA | NA NA | ee | ER | 8/20 |
| 5424B | 1.0% | 24 | 0 | 0 | ER | ER | |
| | 1.0 10 | 48 | 0 | | Ru | FP. | 8/18 |
| | | NA. | NA- | NA | | | |
| | | 24 | 1161 | | | 1 | |
| | 1 1 | 48 | | | | | |
| 6410- | 1 / | | | | | 1 | 1 . |
| | 0.4 | NA | NA. | NA. | ER | 88 | 8 26 |
| 1425A | 1001 | 24 | င | 0 | FR | E. | 827 |
| | л 7. (27//2 | /. 2 | | | 1 X 1 X 1 | CO | 0/10 |

NA

0

NA

NA

24

48

6410-

a - Dosage applied by technician indicated

NA - Not Applicable

form change 8/25/81 ER

arecording error 8/25/81 ER

Dose Ranza

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Test Group:

RT No. 87/6010 Veniclesterile 099 Material Varisoft 475 8 Lo+ 1104K

Date Animal Received 5/28/81 Date Initiated 7/3/8/ Source Dean Daul Sex 3

| | | | | | Tech | Rec | |
|------------|------------------------|-------------------------------------|----------|-------|------------------|------------------|------|
| Animal No. | Dose ² (ml) | Obser- vation Period (Hrs) | Erythema | Edema | Technician | Recorded By | 1981 |
| 0240 | 0.5 | NA | NA | NA. | 58 | ER. | 7/13 |
| 0269 | 101 L | 24 48 | NA O | 0 | دو الا الا | R | 7/15 |
| | 0.5 | NA | NA | NA | وو | ER. | 7/13 |
| 0269 B | 0.190 | . 48 | 0 | 0 0 | المر داخ | <u>کر</u> د ک | 7/13 |
| | | NA | NA | NA | | ! | |
| | | 24 | | 1 | | | |
| | | NA | NA. | NA | | | |
| | | 24 | | 1 | | | |
| | | NA | NA. | NA | _ | | |
| | | 24 | | | | | |

a - Dosage applied by technician indicated
 NA - Not Applicable

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Test

| | Test | Grcup: |
|--|------|--------|
|--|------|--------|

RT No. 87 606 Venicle Sterile 0.99 Material Varisoft 475
Saline Lot 1104 K

Date Animal Received 5/28/81

Source Dean Daul Sex 7

Date Initiated 7/13/8/

| | | | | ec | | Rec | |
|------------|------------------------|-------------------------------------|----------|----------|----------------|-------------|------|
| Animai No. | Dose ² (m/) | Obser- vacion Period (Hrs) | Erythema | Ed esse. | | Recorded by | 1981 |
| 0 274 | 0.5 | NA | NA NA | NA | ER. | وع ا | 7/13 |
| 0324 A | 0.1% | 24 48 | <i>9</i> | 0 | . J. S.G |) パ SU | 7/14 |
| | 0.5 | NA | NA | NA | ۶ę. | FR | 7/13 |
| 0324 B | 0.1901 | . 4 8 | 00 | 00 | <u>م</u> 30 | - ₹ | 7/14 |
| | | AK | AK | . NA | | i | |
| | | 24 | | | | | |
| | | KA | NA | NA | | | |
| | | 24 48 | | 1 | | 1 | • |
| | | NA | NA. | NA | | ! | |
| | | 24 48 | | | | | |

a - Dosage applied by technician indicated

NA - Not Applicable

1

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

| $\overline{\mathbf{z}}$ | Test Group: | RT No. 87/606 Vehicles |
|-------------------------|-------------|------------------------|

terile 099Material Varisoft 475: Lot 1104K

5/28/81 Date Initiated Source Dear Daul

| 6410 - Animal No. | Dose ⁴ (ml) | Obser- vation Period (Hrs) | Erythems | Ed ema | Technician | Recorded By | Date 1981 |
|----------------------|------------------------|-------------------------------------|----------|--------|------------|-------------|--------------|
| | 0.5 | NA | NA | MA | S e | ER | 7/9 |
| 0314 | 1.0% | 24 | 0 | 0 | ATA | 1 se | า เอ าไท่ |
| | 0.5 | NA. | NA | NA | FR | عرع | 17/9 |
| 0314 B | 5.0% | 24 48 | 1.0 | (, o | ER MAR | er We | 7/10 |
| | | N A | AK | · NA | | i | |
| | | 24 48 | | 1 | | | |
| • | | NA | NA | NA | | | - |
| | | 24 4 8 | | 1 | |) 21 1 \ | <u> </u> |
| | | NA | NA | NA | | | |
| | | 24 48 | | | | | |

a - Dosage applied by technician indicated
 NA - Not Applicable

Dose Ratize

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

| \boxtimes : | e | 5 | t | Gr | oup | : |
|---------------|---|---|---|----|-----|---|
|---------------|---|---|---|----|-----|---|

Test
RT No. 871606 Venicle Sterile 0.90 Material Varisoff 47

saline

Lot 110.4 K

| Date Animal Received | 5/28/81 | | |
|----------------------|---------|----------------|--------|
| Source Dan Dau | Sex 3 | Date Initiated | 7/9/81 |

| | | | | | [ec] | Reco | L. |
|------------|-------------------|-------------------------------------|----------|----------|----------|--|----------------|
| Animal No. | Dose [®] | Obser- vacion Period (Hrs) | Erythema | Ed ema | nician | Recorded By | 1981 |
| | 0.5 | KA | NA | NA | ER | ER | 79 |
| 029/02 | 771 | 24 | | 1 0 | 1 HJQ | 1 58 | 7110 |
| (A) | 5.0% | 48 | 1 0 | 1 0 | | WR_ | 7/1 |
| 0296 | 0.5 | NA | 8A | MA | ER | FR | 7/9 |
| 10296 | 1.0% | 24 | 1 1.0 | 1 1.0 | 1 68 | EE | 7110 |
| 0296 | 1.0% | 48 | <u> </u> | 0 | 1 M2 | WR | 7/11 |
| | | AK | NA | · NA | | | |
| | | 24 | | <u> </u> | | <u>: </u> | |
| | | <u>48</u> | | ! | <u> </u> | : | |
| | | NA | NA. | . NA | | | - 2 |
| | | 24 | | 1 | <u> </u> | - | |
| | <u> </u> | 48 | i | | <u>.</u> | 1 1 | 1 |
| | i | MA | . TA | NA | | | |
| | | 24 | | | | <u> </u> | |
| 1 | † | 48 | | 1 | ! | <u> </u> | |

a - Dosage applied by technician indicated NA - Not Applicable

P.O. Box 7545 • Madison Wisconsin 53707 • 608/241-4471

A Division of Raiston Purina Company

TLDUBL

MR FOREED L. HARRISON SHIBER CHEMICAL COMPANY, INC. D.O. 101 546 DUPLIS, 0H 43017

RT LAB NO. 871607

ENTERED 05/16/81

REPORTED 09/18/81

/ARISORT 475: LOT 195-136

FURCHACE ORDER WUMBER 021-49378

ENCLOSED:

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

(MODIFIED CLOSED FATCH TECHNIQUE) - METHOD, SUMMARY

RAW DATA ATTACHED

BARY W. THOMPSON, BS

MANAGER, ACUTE TOYICOLOGY

BY AND MOR MALTECH SCIENTIFIC TERVICES, INC.



PO Box 7545 • Madison Wisconsin 53707 • 608/241-4471

A Division of Raiston Purina Company

145 Y"YPER 971607-

35RI70FT 47F: 10I **195-1**36

PRIMALITIER O KIND

DEUMCTIVE: TO DETERMINE THE DELAYED CONTACT HYPERSENSITIVITY FOTENTIAL OF A TEST MATERIAL IN GUIVEA FIGS.

PAGE

TEST ANDHAL: TWENTY-FOUR ACCLIMATED GUINEA PIGS, WEIGHING FROM 322 TO 402 G WEIGH USED FOR THIS STUDY. THE ANIMALS WERE DIVIDED INTO TWO GROUPS TONSISTING OF A NAIVE CONTROL GROUP OF FOUR GUINEA PIGS AND A TREATED GROUP OF TWENTY GUINEA PIGS. AN EQUAL NUMBER OF MALE AND FEMALE ANIMALS WERE PLACED IN EACH GROUP. THE ANIMALS WERE IDENTIFIED BY ANIMAL 'UMBER AND FIG TAG. THE ANIMALN WEEF INDIVIDUALLY HOUSED IN SCREEN-BOTTOM CAGES IN TEMPERATURE AND HUMIDITY CONTROLLED ROOMS. ANIMALS WERE PROVIDED CONTINUOUS ACCESS TO PURINA GUINEA FIG CHOW AND WATER THROUGHOUT THE STUDY PERIOD.

PREPARATION OF TEST MATERIAL: TO PREPARE A 1.0% WEIGHT/VOLUME MIXTURE, 1.0 GOF VARISOFT 475: IOT 195-136 WAS WEIGHED INTO AN ERLENMEYER FLASK. STERILE 0.0% SALINE WAS ADDED TO MAKE A TOTAL VOLUME OF 100 ML. THE MIXTURE WAS THEN STIRBED MSING A STIR PLATE AND A MAGNETIC STIR BAR TO A UNIFORM SUSPENSION. THE TEST MATERIAL WAS PREPARED FRESH PRIOR TO EACH APPLICATION.

TREATMENT: THE DAY BEFORE EACH APPLICATION THE HAIR WAS REMOVED FROM THE LEFT SHOULDER OF EACH ANIMAL WITH ELECTRIC CLIPPERS. THE TEST MATERIAL WAS APPLIED TO ONE AREA ON EACH ANIMAL BY PLACING 0.4 ML OF THE FRESHLY PREPARED 1027 SUBSTANCE ON A REBRIL PAD (7/8 INCH X 1 INCH) AND PLACING THE PAD ON THE TEST SITE ALONG THE MIDLINE OF THE BACK. THE PATCH WAS COVERED WITH PURPER DAM AND SECURED WITH AN OVERWRAP OF ELASTOPLAST TAPE. THE DRESSING REMAINED IN PLACE FOR A PERIOD OF SIX HOURS AT WHICH TIME IT WAS REMOVED. THE TEST MATERIAL WAS REMOVED BY A GENTLE RINSE WITH WARM WATER BEFORE RETURNING THE ANIMALS TO THEIR CAGES.

THE ANIMALS RECEIVED ONE APPLICATION PER WEEK FOR THREE WEEKS FOR A TOTAL OF THREE APPLICATIONS.

TWO WEEKS FULLOWING THE ADMINISTRATION OF THE THIRD SENSITIZING DOSE, A CHALLENGE DOSE AT A VOLUME OF 0.4 ML WAS ADMINISTERED TO THE TEST GROUP IN THE SAME MANNER AS DURING THE SENSITIZING PHASE OF THE STUDY. AT THIS TIME, I'VE FOUR NAIVE (PREVIOUSLY UNTREATED) CONTROL ANIMALS WERE ALSO TREATED WITH CHALLENGE APPLICATIONS WERE MADE TO A FRESHLY CLIPPED EKIN SITE THAT HAD NOT PEEN PREVIOUSLY TREATED. TWENTY-FOUR HOURS AFTER PRIMARY CHALLENGE, THE ANIMALS WERE DEPILATED WITH NEET CREAM HAIR ELMOVER (WHITEHALL LAPORATORIES, INC., NEW YORK). THE DEPILATORY WAS APPLIED ON THE TEST LITES AND SURROUNDING AREAS FOR 30 MINUTES. THEN THE DEPILATORY WAS THOROUGHLY WASHED OFF WITH WARM WATER, THE ANIMALS DRIED WITH I TOWEL AND FETURNED TO THEIR CAGES.



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LAR MUMBER 971607-

PAGE 3

(NEID >FP 475: ICF 195-13)

(CONTINUED) WILLELLISMEN

OBSERVATIONS: THE APPLICATION CITES WERE READ AND SCORED FOR ERYTHEMA AND EDEMA AT 24 AND 48 YOURS FOLLOWING EACH APPLICATION DURING THE SENSITIZING PHADE OF THE DIUDY. REACTIONS TO THE CHALLENGE DOSE WERF REAL AND SCORED TWO YOURS AFTER DEPILATION AND 24 HOURS LATER (48 HOUR SCORES). THE ANIMALS ENTIFE OBSERVED FOR GRIERAL BEHAVIOR AND APPEARANCE ONCE DAILY TURING THE ENTIFE STUDY PERIOD BODY WEIGHTS WERE TAKEN AT STUDY INITIATION AND AT WEEKLE INTERVALS DURING THE STUDY.

PATHOLOGY: AT STUDY TERMINATION ALL ANIMALS WERE EUTHANATIZED AND DISCARDED.



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A Division of Raiston Purina Company

T LAP (UM2F) 971607-

PAGF 4

TARISTED 47%: IND 195-136

(KIN DEBUTTITATION (CONTINUED)

TEUT ANIMAL: GUINEA PIGS

SOUTTE: DEAN DAUL, LUIEMBURG, WIDATE ANIMALS RECEIVED: 7/10/81

DATE FEST STARFED: 7/22/81

DATE TEST COMPLETED: 8/21/81

SUMMAPY OF SKIN REACTEONS**

TEST GROUP - MALES

| SENSITIZING PHASE | | | CHATITURE DULLE | | | | | | | |
|---------------------------|--------------|----------|-----------------|--------|-----------------|-------------|--------|--------|--|--|
| | | | | | CHALLENGE PHASE | | | | | |
| | T | HPEE APP | LICATI | ONS | 2 | INGLE AF | FLICAT | TON | | |
| ANIMAL | FRY | THEMA | ED | EMA | | THEMA | EDEMA | | | |
| "UMBER | AVE. | (HIGH) | AVE. | (HIGH) | AVE. | (HIGH) | AVE. | (HIGH) | | |
| 54100383 | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | | |
| 54100334 | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | | |
| 54100384 | 3.0 | (0) | 0.0 | (0) | 0.3 | (0.5) | 0.0 | (0) | | |
| 64100357 | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | | |
| 64 1 00388 | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | | |
| 54 1 00393 | 0.0 | (0) | 0.0 | (C) | 0.0 | (0) | 0.0 | (0) | | |
| 54 1 1 0 3 3 0 | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | | |
| ¥100396 | 0 . C | (O) | 0.0 | (0) | 0.0 | (0) | 3.0 | (0) | | |
| 541∈6391 | 0.0 | (C) | 0.0 | (0) | 0.0 | (0) | 0.3 | (0) | | |
| 54100392 | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | | |
| | | | | | | | - | | | |
| MAIVE CONTROL | | | | | | | | | | |
| 641003F2 | | UNTREATE | D | | 0.0 | (0) | 0.0 | (0) | | |
| 64100398 | ! | UNTREATE | D | | 0.0 | (0) | 0.0 | (0) | | |
| | | | | | | * * * * * * | a' | , | | |

^{**} THE - VERAGE ERYTHEMA AND EDEMA VALUE IS THE MEAN SCORE FOR THE SIX OBSERVATIONS (SENSITIZING TREATMENT) OR TWO OBSERVATIONS (CHALLENGE TREATMENT)
OF THE APPLICATION SITE FOR EACH ANIMAL. THE HIGH READING IS THE HIGHEST SCORD RECORDED FOR THE RESPECTIVE ANIMAL DURING THAT PHASE OF THE STUDY.



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T TAP MINERA 871607

PAGE 5

)

VARIFORD 475: LOT 195-136

OKIV OFVETTICATION (CONCINUED)

TEST ANIMAL: GUINEA PIGS

SOUFCE: DEAN LAUL, LUMEMBURG, RIDATE ARIMALS RECEIVED: 7/10/81

DATE TEST STARTED: 7/22/81

DATE TEST COMPLETED: 8/21/81

SUMMARY OF SKIN REACTIONS** (CONT.):

TEST GROUP - FEMALES

| | | | | | | - | | |
|-------------------|------|----------|--------|--------|-------|----------|------|-------|
| | | FASITIZI | | | CH | FALLENGE | HASE | |
| | TH | REE APPI | ICATIO | NS | | GLE APPI | |) N |
| ANIMAL | ERY | THEMA | EDE | AM? | | THEMA | EDE | |
| NUMBER | AVE. | (HIGH) | AVE. | (HIGH) | A VE. | (HIGH) | AVE. | (HIGH |
| 64100433 | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) |
| 54100434 | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) |
| 64100435 | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) |
| 64100435 | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) |
| 54100437 | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) |
| 64100436 | 0.0 | (0) | 0.0 | (0) | 0.0 | (c) | 0.0 | (0) |
| 64 1 00439 | 0.0 | (C) | 0.0 | (0) | 0.0 | (0) | 3.0 | (0) |
| 100446 | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) |
| -100441 | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) |
| 64100442 | 0.3 | (O) | 0.0 | (0) | 0.3 | (0.5) | 0.0 | (0) |
| | | | | | | | | |
| | | | | | | | | |
| MATUT CONTLO | ▼ | | | | | | • | |
| NAIVE CONIRC | L | | | | | | | |

| N | łΙ | ٧ | Ξ | C | ΰ | ١ | Ι | kС | L |
|-----|-----|--------|----|---|---|---|---|----|---|
| £ 1 | . 4 | \sim | 00 | | _ | | | | |

| 64100445 64100446 | UNTREATED UNTREATED | | | 0.0 | |
|----------------------|------------------------|-----|-----|-----|-----|
| • | 0 12 11 12 11 12 12 | 0.0 | (0) | 0.0 | (0) |

^{**}THE AVERAGE ERYTHEMA AND EDEMA VALUE IS THE MEAN SCORE FOR THE SIX OBSERVA-TIONS (SENSITIZING THEATMENT) OR TWO OBSERVATIONS (CHALLENGE TREATMENT) OF THE TEST SITE FOR EACH ANIMAL. THE HIGH READING IS THE HIGHEST SCORE RECORDED FOR THE RESPECTIVE ANIMAL DURING THAT PHASE OF THE STUDY.

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TT LAB FUMBEL 971607-

"APISORT 478: LOT 195-136

PAGE 5

TRIN COMULTURATION (CONTINUED)
- EFOULTS:

GEMERAL BEHAVIOR AND ALTEARANCE: ALL OF THE GUINEARPIGS USED IN THIS STUDY AFPEABED MORMAL THEOUGHOUT THE STUDY PERIOD. NORMAL BODY WEIGHT GAINS WERE RECORDED FOR ALL ANIMALS DURING THE COURSE OF THE STUDY.

SKIN REACTIONS TO VARIDORT 475: LOT 195-136 (1.0% W/V AQUEOUS):

ONE MALE (NO. 64100315) AND ONE FEMALE (NO. 64100442) REACTED TO THE CHALLENGE APPLICATION WITH A VERY FAINT NONCONFLUENT ERYTHEMA AT THE 24 HOUR OBSERVATION. BOTH OF THE RESPONSES WERE NOT SUBSTANTIAL ENOUGH TO BE CONSIDERED POSITIVE FOR SENSITIZATION.

.NCLUSION:

REPORTSE NO SENSITIZATION WAS DETECTED IN THIS STUDY, THIS TEST MATERIAL IS NOT CONSIDERED A STRONG SKIN SENSITIZER.

Dermal Sensitization in Guinea Fig.

Sterile

Test Group RT No. 8711007 Vehicle 0.990 salineTest Compound Varisoft 475

Lot 195-130 NA Positive Control Group NA Vehicle NA

| _ Jex | <u> </u> | | | | | | | | |
|---------------|---------------|----------------|---------------|---------------|---------------|---------------|---------------|-----------------|--------------|
| | | | Animal | Number | | | | | |
| 6410- 0383 | 6410- 6384 | 6410 - 0385 | 6410- 0387 | 6410- 0388 | 6410- 0395 | 6410- 0390 | 6410- 0396 | Tech- nician | Date 1981 |
| 359 | 383 | 379 | 3 68 | 373 | 398 | 402 | 398 | EP. | nlaa |
| 444 | 437 | 463 | 413 | 453 | 447 | 493 | 4107 | | |
| 528 | 506 | 540 | 789 | 198 | 520 | 573 | 539 | JR | 8/5 |
| 600 | 556 | 606 | 0544 | 532 | 581 | 655 | 598 | Dh | 8/12 |
| 669 | 617 | 645 | 599 | 565 | 631 | 706 | 648 | EL | 8/19 |
| | | | | | | | | | |

| | | Animal Number | | |
|---------------|---------------|--------------------------|-----------------|-------------|
| 6410- 0391 | 6410- 0392 | | Tech- nician | Date 198 |
| 391 | 393 | Scale Used: K. Tron 4809 | ક્ર | , |
| 481 | 493 | Scale Used: K-TRON 4809 | del | 7/29 |
| 553 | 558 | Scale Used: K-TRON 4809 | IR | 8/5 |
| 642 | 633 | Scale Used: IC TRON 4809 | De | Rlia |
| 719 | 700 | Scale Used: Ktrox 4809 | ER. | 8/19 |
| | | Scale Used: | | / |

NA - Not Applicable

1) Recording error 8/12/81 DL

Dermal Sensitization in Guinea Pigs - Daily Observations Sterila

Test Group RT No. 871607Vehicle 0.990 saline Test Compound Varisoft 475:

WA Positive Control Group NA Vehicle NA Room No. 2

| | oex C | Án. | imal Numb | er | | | | 1 | |
|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|-----------|--------------|
| 6410- 0383 | 6410- 0384 | 6410- 0385 | 6410- 0387 | 6410- 0388 | 6410- 0395 | 6410- 0390 | 6410- 0396 | | Date /98/ |
| N | N | N | N | N | N | N | N | E.P. | 7 22 |
| N | N · | 2 | N | N | N | N | N | ۶۶ | 7/23 |
| N | N | N | N | N | N | - 71 | N | JR | l l |
| N | N | N | N | N | N | N | N | R | 7/25 |
| √ | N | N | N | N | N | N | N | IK | 7/26 |
| N | N | N | Ν | Λ/ | \mathcal{N} | N | N | JR | 7/27 |
| N | N | N | M | N. | N | N | /\/ | NS | 7/28 |
| | N | N | r/ | \sim | 11/ | 1/ | /\ | NOV | 7/29 |
| 2 | 2 | 2 | 7 | 2 | 2 | ? | N | m | 7/30 |
| N | N | V | N | 7 | N | N | N | VDV | 7/31 |
| 2 | N | 2 | 2 | 2 | 2 | 2 | ·N | dh | 8/ |
| | 2 | 2 | N | 2 | 2 | N | N | mo. | 8/2 |
| 2 | 2 | \sim | \sim | \sim | \sim | \sim | N | دلدا | 8/3 |
| N | N | N | μ | N | N | N | N | <i>CD</i> | 8/4 |
| N | N | N | N | N | N | N | N | R | 8/ |
| N | N- | - N | N | V | N . | N | N | NON | 816 |
| N | N | N | N | N | N | N | N | ER | 8/7 |
| \mathcal{N} | 1 | N | N | N | \sim | N | N | R | 9/8 |

N - No Visible Abnormalities

NA - Not Applicable

Dermal Sensitization in Guinea Pigs - Daily Observations Sterile

Test Group RT No. 871607 Vehicle 0.990 salineTest Compound Varisoft 475:

NA Positive Control Group NA Vehicle NA Room No. 2

| <u> </u> | Dax é |)` | | | | | _ | |
|------------|---------------|----|-----------|----|------|---------------------------------------|-----------------|--------------|
| | | | imal Numb | er | | | | |
| 0391 | 6410- 0392 | | | | · | · | Tech- nician | Date 1981 |
| N | N | | | | | | GE. | 7 22 |
| N | N | | | | | | . BR | 7/23 |
| N | N | | | | | | 火 | 7/24 |
| N | N | | | | | | R | 7/25 |
| 1 | N | | | | | • | JR | 7/26 |
| N | N | | | | | | IR | 7/27 |
| N | N | | | | | | 150 | 7/28 |
| N | N | | | | | | NA | 7/29 |
| 2 | 2 | | | | | · | m | 7/30 |
| N | Ν | | | | | | Sav | 7/31 |
| 2 | N | | | | | | 270 | 8/1 |
| \ <u>\</u> | 2 | | | | | | M | 8/2 |
| N | <i>\\</i> | | | | | | Typ | 8/3 |
| N | N | | | | 1000 | \ | IR | 8/5 |
| N | N - | - | | | | \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ | SCN | 86 |
| Ν | N | · | | | | | | |
| N | N | | | • | | | ER. | 8/7 3/8 |

N - No Visible Abnormalities

NA - Not Applicable

Dermal Sensitization in Guinea Pigs - Daily Observations
Sterila Test Group RT No. 871607Vehicle 0.990 Saline Test Compound Varisoft 475: Positive Control Group <u>NA</u> Vehicle <u>NA</u> Room No. 2 Sax 3

| | | | imal Numb | er | | | |] | |
|---------------|-------|---------------|----------------|---------------|---------------|---------------|---------------|-------|--------------|
| 6410- 0383 | 6410- | 6410- 0385 | 6410 - 0387 | 6410- 0388 | 6410- 0395 | 6410- 0390 | 6410- 0396 | | Date /98/ |
| N | N | N | N | N | N | N | N | P | 8/9 |
| 7 | 2 | ريو | N | N | N | \sim | ν. | da | 8/10 |
| Λ/ | N | \mathcal{N} | N | N | N | \wedge | N | JR. | 8/11 |
| N | N | | N | ~/ | . N | A. | 41 | DR | 8/12 |
| N | _ N | N | N | Ŋ | N | N | N | ER. | 8/13 |
| N | N | N | N | N | N | (Vr | N | ded | 8/18/4 |
| N | N | . ~ | | N | N | N | N | oll | 8/15 |
| N | N | N | Ń | Ŋ | N | N | N | derik | 8/16 |
| N | N | ·N | N | N | N | N | N | da | 8/17 |
| 7 | N | \sim | N | N | N | N | N | DA | 8/18 |
| N, | N | N | N | N | N | N | N | ER | 8/19 |
| N | N | <i>λ</i> : | N) | N | ω | N | N | de | 8/20 |
| N | N | N | N | N | W | N | N | ER | 8/21 |
| | | | | | | | | | |
| | | | | | | | | | |
| | _ | - | , | | | | | | |
| | | | | | | | | | |
| | | | | | | | | | |

N - No Visible Abnormalities

NA - Not Applicable

(1) Recording Error des 8/14/81
(4) Recording Error des 8/17/81

Dermal Sensitization in Guines Pigs - Daily Observations Sterile

Test Group RT No. 871607 Vehicle 0.990 salineTest Compound Varisoft 475 Positive Control Group NA Vehicle NA Room No. 2

| | Dex (| <u>6</u> | | | | | | | |
|---------------|---------------|----------|-----------|------|----------|----------|--------------|-----------------|--------|
| | | | imal Numb | er – | | | | | |
| 6410- 0391 | 6410- 0392 | | | | · | · | | Tech- nician | Date |
| | | | | | | | | | 1981 |
| N | N | | | | | | | JP | 8/9 |
| | N | | | | | | | dole | 8/1n |
| | 1 | | | - | | | | JR | 8/11 |
| N | N | | | | | | | Da | |
| N | N | | | | | | | ER | 8/13 |
| N | N | | | | | | | dw | 8/13/4 |
| ~ | N | | | | | | | - DA | 8/15 |
| N | N | | | | | | | W JUNE | 8/16 |
| N | 2 | | - | | | | | da | 8117 |
| 2 | 7 | | | | | | | DA | 8/18 |
| N | N | | · | | | | 3 | ER | 8/19 |
| N | ω | | | | | t | | de | 8/20 |
| N | N | | | | | | | ESC | 8/21 |
| | | | | | | | | OOC | |
| | | | | | | | | - | • |
| | | - | • | | | | | | |
| | | • | | | <u>-</u> | | \ | | |
| | | | | | | | _ | | |
| | | <u> </u> | | | | | | | |

N - No Visible Abnormalities

NA - NOE Applicable Decoelife Eppendous/14/8

(a) Power Nos Mile (18 81)

(a) Precording error 8/21/8

| | DERMAL | SENSTITZATIO | N START TH COT | NEA PIGS | • | | | |
|------------------------------|------------------------|-------------------------------------|----------------|----------|------------|-------------|-------------|-------|
| | | | 607 Venica | | Line Mat | erial \ | Lot | 195- |
| NA Posi | tive Contro | l Group | Vehic | :le _NA | An | imal N | 6410 | 383 |
| ate Animal | Received _ | | | | Date | Initi | ated _ | nlaal |
| ource De | an Daul | Sex | 3 | | Chall | enge I | ate _{ | 3/19/ |
| | • | | | | | | | 1 |
| | | | | T | ecjus. | Recor | Date | |
| Sensi- tizing Dose No. | Dose ² (mi) | Obser- vacion Period (Hrs) | Erythema | Edema | cian | Recorded By | 1981 | |
| • | 0.4 | . NA | NA ' | NA | R | P | 7/22 | |
|] | | 24 48 | 0 | ာ () | MAR | 23 JR | 7/24 | |
| | 0.4 | NA | NA | NA | ACIN | | | |
| a . | | . 24 . 48 | 00 | Co | N20 | 77 | 7/30 | |
| | 0.4 | NA | NA | NA | DA | De | \$ 5 | |
| 3 | | · 24 | Co | 00 | ALX) EE | MX) ER | 8/0 | |
| Challenge | 0.4 | NA | NA | NA | 52 | ER | 8/19 | |
| Dose | | 24 | 0 | 0 | + 58. | de | 8/20 8/4 | |
| | | | | | | 1 | . 7 | |

24 48

a - Dosage applied by technician indicated
 NA - Not Applicable

| Test Group: | RT No. 871607 | Vehicle 0.9% salin | Test EMaterial Vori | saft 47 |
|----------------------|---------------|--------------------|------------------------|---------|
| NA Positive Control | Group NA | Vehicle NA | | |
| Date Animal Received | 7/10/81 | _ | Date Initiated | ग्रह्मा |
| Source Dean Day | Sex <u>3</u> | c | hallenge Date | 8 19 81 |

| | • | | | | Tech | Rec | _ |
|------------------------------|-------------------|-------------------------------------|----------|-------|--------|-------------|------|
| Sensi- tizing Dose No. | Dose ² | Obser- vation Period (Hrs) | Erythema | Edema | nician | Recorded By | 1981 |
| • | 0.4 | na | NA | NA | R | 137 | 7/22 |
| 1 | | 24 | 0 | 0 | JAK . | . E | |
| | | 48 | 0 | 0 | 18 | ir | |
| ~ | 0.4 | NA | NA. | NA | NIV | RW | 7/29 |
| a a | | 24 | | 0 | dul | عومر | 7/30 |
| | | 48 | | 0 | 100 | 1001 | 131 |
| 2 | 0.4 | NA. | NA. | NA | 12 | Sa | 85 |
| 3 | | . 24 | | 0 | 140 | 11/20 | 810 |
| | | 48 | 0 | 0 | ER | ER, | 8/7 |
| Challenge | 0.4 | NA | NA . | NA. | ٤٤ | ER | 8/19 |
| Dose | | 24 | D | 0 | ER | | 5/20 |
| | | 48 | 0 | 0 | SR | de | 8/21 |
| | | MA | MA | NA | • • | ÷" | |
| | | 24 | | | | | |
| | | 48 | | | | | |

a - Dosage applied by technician indicated NA - Not Applicable

| | DERMAL S | ENSITIZ | ATION ST | CABA IN | GUINEA | PIGS | • | |
|-----|----------|---------|----------|---------|-----------------------|---------------------|--------------------------------|---------------------|
| ر | _p: | RT No. | 8716 | | st hicle <u>Q.</u> | eri le 196 salio | Test EMaterial Vori: Lot | saft 475 195-136 |
| ive | Control | Group _ | NA | v | ehicle _ | NA | Animal No | 0385 |
| Rec | eived | .7/10 | 181 | | | | Date Initiated | 7/22/81 |
| | Daul | | | _ | • | 1 | Challenge Date | 8/19/81 |

| | | 1 | | Tech | Rec | 2 |
|------------------------|-------------------------------------|------------|----------------|----------|-------------|--------------|
| Dose ² (ml) | Obser- vation Period (Hrs) | Erythema ' | Edema | hnician | Recorded By | 1981 |
| 0.4 | NA | RA | NA | JP | R | 7/12 |
| | 24 | 0 | 0 | MAN | ER | 7 23 |
| | 48 . | 0 | 0 | I.C. | IK | 7 /24 |
| 0.4 | NA | NA | NA | MM | NZV | 7/29 |
| | 24 | 0 | | de | au | 1/30 |
| | . 48 | 0 | 0 | 120 | 120 | 7/31 |
| 04 | NA | NA | NA | TR | 128 | 815 |
| | 24 | | $\downarrow Q$ | VOX | NX) | 8/10 |
| | 48 | 0 | | ξ₿. | ER. | 8/7 |
| 0.4 | NA | NA | NA | ٤٤ | ER | 8/19 |
| 1 | 24 | 0.5 | 0 | ER. | de | 5/20 |
| | 48 | 0 | 0 | 56 | da | 8/21 |
| | - 184 | MA | NA. | | <u> </u> | |
| | 24 | | | 4 | | |
| II | 48 | | | <u> </u> | | |

applied by technician indicated plicable

| Test Group: | RT No. | 87160 | ☐ Vehicle Ç | iteri le 1.9% salion | Test EMaterial Vo | risof | <u>+ 475</u> 15-13 |
|----------------------|----------|-------|-------------|-------------------------|----------------------|------------|-----------------------|
| NA Positive Control | | NA | Vehicle | NA | _ Animal No | 6410- | تع |
| Date Animal Received | 7/10 | 181 | | | Date Initia | ted 7/ | عادد |
| Source Dean Day | <u> </u> | _ Sex | <u> </u> | | hallenge Da | e <u>8</u> | 19/81 |

| | .* | | | | | | |
|------------------------------|---------------------------|-------------------------------------|----------|-------|--------|-------------|------|
| Sensi- tizing Dose No. | Dose ² (ml) | Obser- vation Period (Hrs) | Erythema | Edema | nician | Recorded By | 1981 |
| • | 0.4 | NA | NA | NA | R | R | 7/22 |
| l | | 24 | 0 | 0 | M | EP | 7123 |
| | | 48. | 0 | 0 | IC | JP | 7/24 |
| | 0.4 | NA | NA. | NA | NX | NON | 7/29 |
| a | | 24 | 0 | 0 | dh | 140 | |
| | | · 48 | 0 | 0 | 122 | 100 | 7,31 |
| 2 | 0.4 | na | NA | NA | Da | Na | 215 |
| 3 | | . 24 | 0 | | | MAX | 8/1 |
| | | 48 | ٥ | 0 | 82 | EP | 87 |
| Challenge | 0.4 | NA. | NA . | NA | 50 | 50 | 8/19 |
| Dose | | 24 | 0 | 0 | 68 | dei | 9/20 |
| | | 48 | 6 | 10 | દ્રષ્ટ | da | 8/21 |
| | | MA | NA | NA | | | |
| | [| 24 | | | | | |
| | | 48 | L | | | | |

a - Dosage applied by technician indicated NA - Not Applicable

| Lest Group: | RT No. 871607 | sterile Vehicle <u>0.9% salir</u> | Test Material Vori: Lot | soft 475: |
|------------------|---------------|--------------------------------------|-------------------------------|-----------|
| Tositive Control | Group NA | Vehicle NA | Animal No. | 0388 |
| Animal Received | 7/10/81 | · • | Date Initiated | 7/22/81 |
| ce Dean Day | Sex <u> </u> | | Challenge Date | 8 19 81 |

| | | . 4 | | | Tech | lec | |
|------------|---------------------------|-------------------------------------|------------|-------|--------|-------------|------|
| si- ing | Dose ⁴ (ml) | Obser- vation Period (Hrs) | Erythema | Edema | mician | Recorded By | 1981 |
| 1 | 0.4 | RA | RA | NA | R | R | 7/22 |
| 1 | | 24 | 0 | 0 | WK | દર | 7123 |
| - | | 48. | | 0 | 15 | JR | 7/24 |
| _ | 0.4 | NA | NA. | NA | NOV | REN | 7/29 |
| ۲ | | 24 | 0 | 0 | Typ | NO | 7/30 |
| | | . 48 | 0 | 0 | 100 | MON | 7131 |
| 2 | 0.4 | NA | NA | NA. | De | Da | 8/5 |
| 3 | | 24 | \bigcirc | | NOV | N. 787 | 8170 |
| - | | 48 | 0 | 0 | S.C. | ER_ | 8 7 |
| ulenge | 0.4 | NA | NA. | NA. | se | se | 819 |
| Sec | | 24 | 0 | 0 | فك | des | 8/20 |
| | | 48 | | 10 | 93 | day | 8/21 |
| | | MA | NA | NA | | | |
| | 1 | 24 | | | | | |
| | | 48 | | | | | |

⁻ Dosage applied by technician indicated - Not Applicable

| Test Group: | RT No. 871607 | Vehicle 0.9% sal | Test DE Material Voris | s oft 475 |
|----------------------|---------------|------------------|---------------------------|----------------------|
| NA Positive Control | Group NA | Vehicle NA | Animal No. | 0395 |
| Date Animal Received | | , | Date Initiated | य्वे व्या |
| Source Dean Day | Sex <u> </u> | | Challenge Date | 8/19/81 |

| | • | | | | Tec | Rec | |
|------------------------------|---------------------------|-------------------------------------|----------|-------|--------|-------------|------|
| Sensi- tizing Dose No. | Dose ⁴ (ml) | Obser- vation Period (Hrs) | Erythema | Edema | nician | Recorded By | 1981 |
| | 0.4 | NA | NA. | NA | R | F | 7/12 |
| 1 | | 24 | | | MY | ER | 7/23 |
| • | | 48 | 0 | 0 | JK | 1/ | |
| _ | 0.4 | NA | NA | NA | NON | VCN | 7/29 |
| a | | 24 | 0 | 0 | 140 | 110 | 7/30 |
| | · | . 48 | Q | 0 | 1200 | NO | 281 |
| 2 | 0.4 | AK | NA | NA | 12 | Dh | 8/5 |
| 3 | | . 24 | 0 | | N(X) | MA | 810 |
| | | 48 | 0 | 0 | ER | ER | |
| Challenge | 0.4 | NA | NA | NA | FQ | FR | 8/19 |
| Dose | | 24 | 0 | 0 | ce. | | 8/20 |
| | | 48 | | 0 | ce | da | 8/21 |
| | | NA . | MA | NA | | ÷" | • |
| | | 24 | | | | | |
| | | 48 | | | | | |

a - Dosage applied by technician indicated
 NA - Not Applicable

| Test Group: | RT No. 871607 | Vehicle 0.9% saline | Test Material Voris | 50 + 47 |
|----------------------|---------------|---------------------|------------------------|---------|
| NA Positive Control | Group NA | Vehicle NA | _ Animal No. C | 390 |
| Date Animal Received | 7/10/81 | <u> </u> | Date Initiated | 1/22/8 |
| Source Dean Day | Sex <u> </u> | · a | nallenge Date | 8/19/8 |

| | 4 | | | | (Tec) | Rec | |
|------------------------------|---------------------------|-------------------------------------|----------|-------|-------------|-------------------|------|
| Sensi- tizing Dose No. | Dose ² (ml) | Obser- vation Period (Hrs) | Erythema | Edema | echnician . | Recorded By | 1981 |
| | 0.4 | NA | NA | NA | R | P | 7/in |
| 1 | | 24 | 0 | 0 | W | se | 7123 |
| | | 48 | 0 | 0 | JK | JK | 7/24 |
| | 0.4 | NA. | NA | NA | NO | 100 | 7/29 |
| l a | | 24 | | 0 | 140 | del | 7/30 |
| | | · 48 | | 0 | 1120 | 1/20 | 131 |
| 2 | 0.4 | NA | NA | NA | Da | De | 8)5 |
| 3 | | . 24 | 0 | | LADX/ | N.M | 810 |
| | | 48 | 0 | 0 | ۶٤. | ER | 817 |
| Challenge | 0.4 | NA | NA. | NA | ٤٤ | ٤٤ | 8/19 |
| Dose | | 24 | ٥ | Q | · 88 | de | 8/20 |
| | | 48 | | 0 | ER. | $(\alpha \alpha)$ | R/A |
| | | NA . | NA | NA | ., | a ^r | |
| | | 24 | | | | | |
| | <u> </u> | 48 | | 1 | | | |

a - Dosage applied by technician indicated
 NA - Not Applicable

| Test Group: | RT No. 871607 | venicle 0.9% sali | Test Material Voris Lot | s oft 47 |
|----------------------|---------------|-------------------|---------------------------|---------------------|
| NA Positive Control | Group NA | Vehicle NA | | |
| Date Animal Received | 7/10/81 | | Date Initiated | 1/22/8 |
| Source Dean Daul | Sex <u> </u> | - | Challenge Date | 8/19/81 |
| | | | | |

| | • | | | | Tech | Rec | |
|------------------------------|------------------------|-------------------------------------|---------------|--------|--------|-------------|------|
| Sensi- tizing Dose No. | Dose ² (ml) | Obser- vation Period (Hrs) | Erythema | Edema. | mician | Recorded by | 1981 |
| • | 0.4 | NA | RA. | NA | R | R | 1/22 |
| 1 | | 24 | 0 | 0 | MP | 82 | 7/23 |
| | | 48 | 0 | 0 |)12 | JK | 7/24 |
| 2 | 0.4 | NA_ | NA. | NA NA | NUN | 100 | 7/29 |
| l a | | 24 | 0 | 0 | del | du | 7/30 |
| | · | . 48 | 0 | 0 | 1130 | 100 | 731 |
| 2 | 0.4 | NA | NA | NA | De | 100 | 8/5 |
| 3 | | . 24 | \mathcal{O} | | M/M | NN | 810 |
| | | 48 | 0 | 0 | ج | ER. | 817 |
| Challenge | 0.4 | KA | NA | , NA | 60 | ER | 8/19 |
| Dose | | 24 | 0 | ρ | . EP | des | 8/20 |
| | | 48 | 0 | Ò | 50 | dei | 8/21 |
| | | NA . | MA | NA. | | ÷' | • |
| | | 24 | | | | · | |
| | | 48 | | | | | |

a - Dosage applied by technician indicated
 NA - Not Applicable

| RMAL S | ENSITIZ# | ATION | STUDY | IN (| JUINEA | PIGS | | | | | |
|--------|----------|-------|----------|------|--------|-------------------|------|--------------|-------|------|-----------|
| : | RT No. | 8710 | 607 | Veh | icle Q | terile 9% sali | Te: | st terial | Varia | oft. | 475. |
| ontrol | Group _ | NA | \ | _ Ve | hicle | NA | A: | nimal | No. | 039 | -136 L |
| ved | 7/10/ | 81 | | | | | Date | e Init | iated | 7/22 | 81 |
| ابيد | | Sex | 3 | | | | Chal | Lenge | Date | 8/19 | 81 |

| | | 1 | Tech | Rec | | | |
|-----|-------------------------------------|----------|-------|-----------------|--|----------|--|
| 1) | Obser- vation Period (Hrs) | Erythema | Edema | nicien | Recorded By | 1981 | |
| + 1 | NA | NA | NA | R | SP | 7/22 | |
| | 24 | | 0 | M/2 | 82 | 7123 | |
| | 48 | 0 | 0 | 16 | IK | | |
| 4 | NA | NA | - NA | NON | NON | 7/29 | |
| | 24 | 0 | 0 | ded | del | 7/30 | |
| , | 48 | 0 | | NZA | 1020 | 181 | |
| 4 | МА | NA | KA | DL | Da | RIS | |
| | 24 | 0 | | $\Delta \infty$ | MXX | 80 | |
| | 48 | 0 | 0 | ER | EZ | 817 | |
| 4 1 | NA | NA | NA | ۶۶ | ER | 8/19 | |
| | 24 | 0 | 0 | se | du | 8/20 | |
| | 48 | 0 | 0 | se | del | 8/21 | |
| | NA | NA | NA | | | • | |
| L | 24 | | | | | <u> </u> | |
| | 48 | | | | | | |

led by technician indicated

ole

| Test Group: | RT No. 871607 | Vehicle 0.990 saling | Test EMaterial Vari | soft 475 |
|----------------------|---------------|----------------------|------------------------|------------------------|
| NA Positive Control | Group NA | Vehicle NA | _ Animal No | 195-131 10- 0392 |
| Date Animal Received | 7/10/81 | - | Date Initiated | 7/22/81 |
| Source Dean Day | Sex <u>3</u> | a | hallenge Date | 8/19/81 |

| | • | | | | iec. | Rec | L |
|------------------------------|------------------------|-------------------------------------|----------|-------|------------|-------------|------|
| Sensi- tizing Dose No. | Dose ² (ml) | Obser- vation Period (Hrs) | Erythema | Edena | Technician | Recorded By | 1981 |
| 1 | 0.4 | MA | RA , | NA | R | R | 7/22 |
| ļ, | | , 24 | 0 | 0 | MAP | ER. | 7123 |
| | | 48 | 0 | 0 | JK | IK | |
| ~ | 0.4 | NA | NA | NA | NO | MM | |
| 2 | | 24 | 0 | 0 | m | 100 | 7/30 |
| | | . 48 | C | 0 | 200 | REN | 281 |
| 2 | 0.4 | NA | AM | NA | Ne | Ne | 815 |
| 3 | | . 24 | | 0 | AZX | KN | 816 |
| | | 48 | Ò | 0 | S.S. | ER | 817 |
| Challenge | 0.4 | NA | NA . | NA. | 5.6 | ER | 8/19 |
| Dose | | 24 | J | O. | . 52 | day | 8/20 |
| | | 48 | Ð | 0 | ٤٤ | de | |
| | | Kes | NA | NA | 14 | انج | |
| | | 24 | | | | | |
| | | 48 | | | | | |

a - Dosage applied by technician indicated
 NA - Not Applicable

Dermal Sensitization In Guinea Pigs - Body Weights

Sterile

Test Group RT No. 871607 Vehicle 0.990 saline Test Compound Varisoft 475:

Lot 195-136 ositive Control Group NA Vehicle NA

| | | | Animal | Number | | | | † | |
|-----------|---------------|--------------|--------|---------------|---------------|---------------|-------|-------|-------|
| 33 | 6410- 0434 | 6410- d35 | 6410- | 6410- 0437 | 6410- 0438 | 6410- 0439 | 6410- | Tech- | Date |
| 75 | 359 | 360 | 380 | 380 | 358 | 374 | 368 | ER | 1981 |
| <u>59</u> | 408 | 427 | 424 | 444 | 400 | 425 | 432 | np | 7/29 |
| 30 | 451 | 492 | 502 | 497 | 436 | 483 | 504 | 18 | 8/5 |
| <u> </u> | 495 | 539 | 554 | 555 | 486 | 537 | Sido | 2 | , |
| 13 | 533 | 596 | 605 | 590 | | 574 | 623 | ER | 8/19 |
| | | | | | | | | C.K | _2114 |

| _ | | Animal Number | | • |
|-----|---------------|--------------------------|-----------------|--------------|
| 141 | 6410- 0442 | | Tech- nician | Date 1981 |
| 73 | 362 | Scale Used: K. Tron 4809 | ER | , |
| | 405 | Scale Used: K-Tron 4809 | عد حد | 7/22 |
| 16 | 434 | Scale Used: K-Tron 4809 | 77 | 8/5 |
| 57 | 471 | Scale Used:)CTRON 4809 | J. | |
| 10 | 527 | Scale Used: K. Tron 4809 | | 8/12 |
| | | Scale Used: | ER | 8/19 |

[·] Not Applicable

Dermal Sensitization in Guines Pigs - Daily Observations

Test Group RT No. 871607Vehicle 0.990 saline Test Compound Varisoft 475 and Positive Control Group NA Vehicle NA Room No. 2

| | , | An | imal Numb | er | | , | | 7 | |
|---------------|---------------|---------------|----------------|---------------|---------------|---------------|---------------|------|--------------|
| 6410- 0433 | 6410- 0434 | 6410- 0435 | 6410°- 0436 | 6410- 0437 | 6410- 0438 | 6410- 0439 | 6410- 0440 | -4-4 | Date 1981 |
| N | N | N | N | N | N | N | N | E.R. | 7/12 |
| N | N | N | N | N | N | 2 | N | ER | 7/23 |
| N | N | N | N | N | N | N | N | JK | 7/24 |
| N | N | N | N | N | N | N | N | R | 7/25 |
| N | N | N | N | N | N | N | N | IL | 7/26 |
| Λ/ | N | N | N | N | N | \mathcal{N} | N | JK | 7/27 |
| | 1/ | 11/ | // | \sim | .// | // | // | 100 | 7/28 |
| Λ./ | 1 | // | 11./ | // | 1/ | ハ | $\Lambda/$ | 100 | 7/29 |
| Ν | \sim | \sim | ·N | N. | N | N | N | del | 7/30 |
| N | N | N | N. | N | N | N | N | rcu | 1/31 |
| 2 | N | 2 | 2 | 2 | 2 | N | 8N | gyp | 8/ |
| N | N | N | N | 2 | 2 | \sim | 2 | dri | 8/2 |
| 2 | 2 | 2 | \sim | N | \sim | N | 2 | che | 8/3 |
| h | N | η | μ | N | N | N | N | CD | 8/4 |
| N | N | N | N | N | N | N | N | R | 8/5 |
| <i>N</i> | N_{-} | N | N | N | N | N | N | NDA | 816 |
| N | N | N | N | N | N | N | N | E.R. | 2/7 |
| N | N | N | N | N | N | N | N | F | 8/2 |

N - No Visible Abnormalities

NA - Not Applicable

Dermal Sensitization in Guines Pigs - Daily Observations
Sterile Test Group RT No. 871607 Vehicle 0.990 salineTest Compound Varisoft 475: Positive Control Group NA Vehicle NA Room No. 2

| | | An | imal Numb | er | | | | 7 | |
|----------|----------------------|----|---------------|----------|-----|---|------------------|-----------------|--------------|
| 6410- | 6410- 0442 | | | | | · | | Tech- nician | Date 1981 |
| N | N | | | | | | | ER | 7/22 |
| N. | N | | | | | | | ER | 7/23 |
| N | N | | 1 | | | | | JK | 7/74 |
| N | 1 | | $\overline{}$ | | | | | JR | 7/25 |
| N | N | | | \ | | | | JK | 7/26 |
| <i>N</i> | N | | | - | | | | IK. | 7/27 |
| N | N | · | | | | • | | NX | 7/28 |
| N | N | | | | | | | 1/77 | 7/29 |
| 22 | N | | • | | | | | np | 7/30 |
| 2 | 2 | | | | | | . _{27.} | NDO | 7/31 |
| 2 | N | | , | | \ \ | | | det | 8/1 |
| N | \sim | | | | | | \ | the shit | 8/2 |
| L) | N | | | | | | | CA | 8/17 |
| N | N | | | | | | | 3P | 3/5 |
| N | N _ | | | | | | | | 86 |
| N | N | • | | | | | | ER | 8/7 |
| N | N | | | | | | | 27 | 813 |

N - No Visible Abnormalities

NA - Not Applicable

tization in Guinea Pigs - Daily Observations

RT No. 871607 Vehicle 0.990 Saline Test Compound Varisoft 475:

repried Group NA Vehicle NA Room No. 2

| An | imal Numb | er | | | | , · · | |
|---------------|----------------|---------------|---------------|---------------|--------------|-----------------|--------------|
| 2410- 2435 | 6410 - 0436 | 6410- 0437 | 6410- 0438 | 6410- 0439 | 0440 0440 | Tech- nician | Date 1981 |
| N | N | N | N | N | N | 3 | 8/9 |
| N | N) | N | 1) | N | N | del | 8/10 |
| _1/ | N | N | N | \mathcal{N} | N | 1/5 | 8// |
| ~ | N | N | N | N | N. | DR | 8/12 |
| -~ | Ν | N | N | N | N | ٤٤ | 8/13 |
| N | N | N | N | N | N | de | 8/14 |
| - ' | N | N | | N | N | 2h | 815 |
| N | N | N | N | N | N | Mark | 8/16 |
| N | N | N | N | . // | N | dw | 8/170 |
| | ~ | | N | N | N | IR | 8/18 |
| N N | - Ń | N | _N_ | N | 6 N | ٤٤ | 8/19 |
| N | N | N | N | N | N | da | 8/20 |
| | N | N | N | N | N | des | 8/21 |
| | | | | | | | |
| | | | | | | | |
| | | | _ | | | | |
| | | | | | | | |
| | | | | | | | |

N - No Visible Abnormalities

MA - Not Applicable
Orecording error 7/21/81 ER
Whending Eller 8/17/8/ da

Dermal Sensitization in Guines Pigs - Daily Observations
Sterile

Test Group RT No. 871607 Vehicle 0.990 salineTest Compound Varisoft 475:
Lot 195-136 Positive Control Group NA Vehicle NA Room No. 2

| | | imal Numb | er | | | | _ | |
|------------------------|---------------|---------------|---------------|---|---|---|-----------------|--------------|
| 0441 | 6410- 0442 | | | | · | | Tech- nician | Date 1981 |
| N | 3 | | | | | | R | 8/9 |
| N | N | | | | | | JR | 8/11 8/11 |
| N | N | $\overline{}$ | | , | | | Da | 8/12 |
| | N | | 1 | | | | se ded | 8/13 8/14 |
| N | \mathcal{D} | | $\overline{}$ | | | · | dair | 8/15 |
| 27 | N | | | 1 | | | 40 | 8/17 |
| N | N | | | | | 5 | SR ER | 8/18 |
| N | N | | | | | | dw. | 8/W 8/21 |
| | | | | | | | | |
| | _ - | | | | | | | |
| | | | | | | | | |

N - No Visible Abnormalities

NA - Not Applicable

Officeoras ERROR SINKI de

| Test Group: | RT No. 87160 | Sterile] Vehicle 0.9% salin | Test Material Vari | s oft 4 |
|----------------------|--------------|-------------------------------|--------------------|--------------------|
| NA Positive Control | Group NA | Vehicle NA | _ Animal No. | 0-136 0-133 |
| Date Animal Received | | | Date Initiated | 7/22/8 |
| Source Dean Day | <u> </u> | a | hallenge Date | 81.918 |

| | | | | | Tec C | Rec | |
|------------------------------|---------------------------|-------------------------------------|----------|-------|---------------------|-------------|------|
| Sensi- tizing Dose No. | Dose ² (ml) | Obser- vation Period (Hrs) | Erythema | Edena | Technician | Recorded By | 1981 |
| | 0.4 | KA | NA | NA | <u>82</u> | EP. | 7/22 |
| | | 24 | 0 | 0 | ive | EP | 7123 |
| | | 48 | C | 0 | JK | JR | 7/24 |
| | 0.4 | NA NA | NA | NA | RCIN | VCN | 7/29 |
| a | | 24 | 0 | 0 | del | gon | 7/50 |
| | | 48 | 0 | 0 | NOW | NTO | |
| 2 | 0.4 | NA NA | NA · | NA | De | N | 25 |
| 3 | | . 24 | \circ | | NTO | MN | 816 |
| | | 48 | 0 | 0 | 58 | EZ | 817 |
| Challenge Dose | 0.4 | NA. | NA. | NA | 50 | ٤٤ | 8/19 |
| Dose | | 24 | 0 | 0 | <i>E</i> 2 . | des | 8/20 |
| | | 48 | <u> </u> | 0 | ·· 66 | dev | 8121 |
| | | WA. | NA | AN | | ÷' | |
| 1 | | 24 | | | • | · | |
| | | 48 | | | | | |

a - Dosage applied by technician indicated NA - Not Applicable

| Test Group: | RT No. | 87160 | Yebicle C | iterile 2.9% salin | Test Material Vari Lot 195 | soft 47 |
|----------------------|---------|-------|-----------|-----------------------|----------------------------------|---------|
| NA Positive Control | Group _ | NA | Vehicle | _NA_ | Animal No. | 043A. |
| Date Animal Received | | 81 | | | Date Initiated | 1/22/81 |
| Source Dean Day | | Sex | <u> </u> | | hallenge Date | 8/19/81 |

| | * | | | | ec. | Rec | |
|------------------------------|------------------------|-------------------------------------|----------|-------|------------|-------------|-------|
| Sensi- tizing Dose No. | Dose ² (ml) | Obser- vation Period (Hrs) | Erytheme | Edema | Technician | Recorded By | 1981 |
| | 0.4 | NA | NA | NA | se. | ٤٤ | 7/22 |
| | | 24 | 0 | 0 | LIE | ER | |
| | | 48 | 0 | 0 | IK | J. | 7/24 |
| | 4 | NA | NA. | NA | NON | NO | 7/29 |
| a | | 24 | 0 | 0 | 740 | 190 | 7/30 |
| | | 48 | C | | M | 120 | 731 |
| 2 | 0.4 | NA | NA. | NA | Ne | DR | 8/5 |
| 3 | | . 24 | | 0 | NCW | NOV | |
| | | 48 | <u> </u> | 0 | 50 | ER | 8 7 |
| Challenge Dose | 0.4 | NA. | NA | · NA | ۶۶ | ٤٤ | છ\ ાવ |
| Dose | | 24 | 0 | 0 | 58 | de | 8/20 |
| | | 48 | 0 | 0 | ٤٤ | da | 8/21 |
| | | NA. | NA | NA | , | ÷ | |
| | L | 24 | | | | | |
| | | 48 | | | | | |

a - Dosage applied by technician indicated
 NA - Not Applicable

| Test Group: | RT No. 871607 | Vehicle 0.990 salin | Test Material Vari Lot 195 | 50ft 4 |
|----------------------|---------------|---------------------|------------------------------|---------|
| NA Positive Control | Group NA | Vehicle NA | _ | |
| Date Animal Received | | _ | Date Initiated | 7/22/8 |
| Source Dean Day | U Sex | <u> </u> | Challenge Date | 8119181 |

| | | | | • | ie C | Rec | |
|------------------------------|-------------------|-------------------------------------|---------------|----------|---------|-------------|------|
| Sensi- tizing Dose No. | Dose ² | Obser- vation Period (Hrs) | Erythema | Edema | nician | Recorded By | 1981 |
| | 0.4 | NA | . NA | NA | SP_ | SE | 7/22 |
|] (| | 24 | 0 | 0 | NVP | ER. | 7/23 |
| | | 48 | . 0 | 0 | JK | IK | 7/24 |
| | 0.4 | NA | NA | MA | NON | NO | |
| a | | . 24 | 0 | 0 | dis | del | 7/30 |
| · | | 48 | 0 | 0 | 100 | 100 | JEAC |
| 3 | 0.4 | NA | NA | NA | Dr | Da | 8/5 |
| 3 | | . 24 | 0 | 0 | NCM | ALX) | 80 |
| | | 48 | 0 | 0 | S.B. | EP. | 8/7 |
| Challenge | 0.4 | NA | NA | NA | દ્ | 50 | 2/19 |
| Dose | | 24 | \mathcal{C} | 0 | EP. | dai | 8/20 |
| | | 48 | 0 | 0 | ` دو | acu | 8121 |
| | | WA | MA | NA | | ÷' | • |
| | | 24 | | | | | |
| | | 48 | | <u>L</u> | | | |

a - Dosage applied by technician indicated
 NA - Not Applicable

| Test Group: | RT No. 871607 | Sterile Vehicle 0.9% salin | Test WMaterial Varisoft 4 Lot 195-136 |
|----------------------|---------------|-------------------------------|---|
| NA Positive Control | Group NA | Vehicle NA | Animal No. 0436 |
| Date Animal Received | | | Date Initiated 7/22/8 |
| Source Dean Day | 1 Sex | | hallenge Date 8 19 8 |

| | | | | | Tec. | Rec | |
|------------------------------|---------------------------|-------------------------------------|---------------|-------|------------|-------------|------|
| Sensi- tizing Dose No. | Dose ² (ml) | Obser- vation Period (Hrs) | Erythema | Edema | echnician | Recorded By | 1981 |
| | 0.4 | - NA | NA. | NA | 58 | çe | 7/22 |
| į į | | 24 | 0 | 0 | Ú. | εR | 7/23 |
| | | 48. | 0 | 0 | JK | JK | 7/24 |
| | 0.4 | NA. | NA | NA | NUN | NOV | 7/29 |
| a | | 24 | 0 | 0 | del | 1340 | 7/30 |
| | | 48 | 0 | | KCU | PCU | 2131 |
| 2 | 0.4 | NA | NA | NA | N | Na | 815 |
| 3 | | . 24 | $\overline{}$ | 0 | NX | 1279 | 80 |
| | | 48 | 0 | 0 | ٤٤ | ER | 817 |
| Challenge | 0.4 | NA. | NA | NA | e e | ER | 8/19 |
| Dose | | 24 | 0 | 0 | ER | da | 8/20 |
| | | 48 | O | 0 | ER | del | 8/2/ |
| | | MA | MA. | NA. | , | ÷' | • |
| | | 24 | | | | 7. | |
| | | 48 | | | | | |

a - Dosage applied by technician indicated NA - Not Applicable

| Test Group: | RT No. 871607 | Vehicle 0.9% salio | Test Material Vari | soft 4 |
|----------------------|---------------|--------------------|---------------------|---------|
| NA Positive Control | Group NA | Vehicle NA | Animal No. | 0437 |
| Date Animal Received | | - | Date Initiated | 7/22/81 |
| Source Dean Dau | 1 Sex 2 | · · · · · | hallenge Date | 8/19/81 |

| | | | | | - | | |
|------------------------------|-------------------|-------------------------------------|----------|-------|--------------|-------------|------|
| Sensi- tizing Dose No. | Dose ⁴ | Obser- vation Period (Hrs) | Erytheme | Edema | Technician | Recorded by | 1981 |
| | 0.4 | NA | NA. | NA | | | |
| | | 24 | 0 | 0 | JWZ- | <u> 60</u> | 7/22 |
| | • | 48 · | | 0 | JK | ER JR | |
| | 0.4 | NA. | NA | NA | NDO | 100 | 7/29 |
| a | | 24 | 0 | 0 | 740 | mo | 7/30 |
| | | 48 | | | NOR | NO | 731 |
| 2 | 0.4 | NA | NA | NA | Da | Na. | 85 |
| 3 | | · 24 | Q | 0 | 1620 | 1/20 | 8/10 |
| | | 48 | D . | 0 | εÞ | EZ | 817 |
| Challenge | 0.4 | , NA | NA | NA. | £ D | ξQ | 8/19 |
| Dose | | 24 | | U | . 82 | de | 5120 |
| | | 48 | | 0 | ER | | 8191 |
| | | WA. | NA | NA | •, | ÷′ | |
| | L | 24 | | | | | |
| | | 48 | | | | | |

a - Dosage applied by technician indicated
 NA - Not Applicable

| Test Group: | RT No. 8716 | O Vehicle | sterile 0.990 salina | Test Material Vari | soft 4- |
|----------------------|-------------|-----------|-------------------------|-----------------------|--------------------|
| NA Positive Control | Group NA | Vehicle | NA_ | Animal No. | |
| Date Animal Received | | | E | ate Initiated | 7/22/8 |
| Source Dean Day | Sex | <u> 오</u> | · Ch | allenge Date | 8/19/81 |

| | | | | • | lec | Re | |
|------------------------------|------------------------|-------------------------------------|----------|-------|------------|-------------|------|
| Sensi- tizing Dose No. | Dose ² (ml) | Obser- vation Period (Hrs) | Erythema | Edema | Technician | Recorded By | 1981 |
| | 0.4 | NA | NA | NA | FR | çe | 7/22 |
| | | 24 | 0 | 0 | We | ٤٤ | 1123 |
| | | 48 . | 0 | 0 | JK | JK | 7/24 |
| | 0.4 | NA. | NA | NA | 1000 | M | 7/29 |
| l a | | 24 | 0 | 0 | 77 | dil | 7/30 |
| | | 48 | | 0 | M20 | NOO | 1810 |
| 2 | 0.4 | NA | NA | NA | ne. | na | 215 |
| 3 | _ | - 24 | | Q | 1670 | N20 | 80 |
| | | 48 | 0 | 0 | ٤٤ | ER | 817 |
| Challenge | 0.4 | NA | NA | NA | 52 | ER | 8/19 |
| Dose | | 24 | 0 | 0 | . 82 | acu | 8/20 |
| | · | 48 | Ð | 0 | EL | de | 8/21 |
| | | NA. | MA. | NA | | # | |
| | <u> </u> | 24 | | | | | |
| | | 48 | | | | | |

a - Dosage applied by technician indicated
 NA - Not Applicable

| Test Group: | RT No. 87160 | St Vehicle Q. | erile 190 salio | Test Material Vari | soft 4 |
|----------------------|--------------|------------------|--------------------|---------------------|---------|
| NA Positive Contro | ol Group NA | Vehicle _ | NA | Animal No. | 0439 |
| Date Animal Received | | · | | Date Initiated | 7/22/8 |
| Source Dean Da | ul Sex 7 | · | | hallenge Date | 8 19 81 |

| | • | | | • | iec C | Rec | |
|------------------------------|------------------------|-------------------------------------|----------|-------|--------------|-------------|------|
| Sensi- tizing Dose No. | Dose ⁴ (ml) | Obser- vation Period (Hrs) | Erythema | Edena | echnicien | Recorded By | 1981 |
| | 0.4 | | NA | NA | 5 R | ۶۵ | 7/22 |
| | | 24 | 0 . | 0 | me | ER | 1123 |
| | | 48. | C | C |)(| JK | 7/24 |
| | 0.4 | NA | NA | NA | NOO | NON | 7129 |
| a | | 24 | 0 | C | del | del | 7/30 |
| | · · | 48 | | | NO | NOO | 7131 |
| 2 | 0.4 | na | NA | NA | DR | Na | \$15 |
| 3 | <u> </u> | · 24 | 0 | | (XCAN | NDN | 810 |
| | | 48 | \sim | 0 | ٤٩. | EL | 817 |
| Challenge | 0.4 | NA | NA . | NA | ۶۵ | 50 | । |
| Dose | | 24 | 0 | Ò | 58 | da | 8/20 |
| | | 48 | 0 | D | ` 5 P | dei | 8/21 |
| | | WA | NA | NA. | | ÷ | • |
| | | 24 | | | | | |
| | | 48 | | | | | |

a - Dosage applied by technician indicated NA - Not Applicable

| Test Group: | RT No. 871607 | Sterile Vehicle 0.9% salin | Test PMaterial Vari | s oft 4 |
|----------------------|---------------|-------------------------------|---------------------|--------------------|
| NA Positive Control | Group NA | Vehicle NA | _ Animal No | 0440 |
| Date Animal Received | | <u>.</u> | Date Initiated | 7/22/8 |
| Source Dean Day | 1 Sex | c | hallenge Date | 8/19/8 |

| | .# | | | | Ē. | 2 | 1 |
|------------------------------|------------------------|-------------------------------------|---------------|------------|------------|--------------|------|
| Sensi- tizing Dose No. | Dose ^d (ml) | Obser- vation Period (Hrs) | Erythema | Edema | Technician | Recorded By | 1981 |
| | 0.4 | NA | NA | NA | FR. | co | |
| } | | 24 | 0 | 0 | we | ER | 7 22 |
| | | 48 | 0 | 0 | IR | JK | 7/24 |
| | 0.4 | NA | NA . | NA | NON | NOO | 7129 |
| a | | 24 | 0 | 0 | Typ | Jy0 | |
| | | 48 | 0 | 0 | NON | WW | 7B |
| 2 | 0.4 | NA | NA | _ NA | N. | Ne | 25 |
| 3 | | 24 | | 0 | ALTO | NO | 80 |
| | | 48 | 0 | 0 | ٤8 | ER | 817 |
| Challenge Dose | C.4 | NA | MA | NA. | ęρ | ER | 8 19 |
| Dose | _ | 24 | \mathcal{O} | ٠ <u>٥</u> | SP | da | 8/20 |
| | | 48 | | 0 | . 56 | da | 8/21 |
| | | HA. | NA | NA | • | 4 | |
| | <u> </u> | 24 | | | | | |
| <u> </u> | | 48 | | | | | |

a - Dosage applied by technician indicated NA - Not Applicable

| Test | Group: | RT No. <u>87</u> | 1607 Vehicl | sterile e <u>0.9%</u> sa | Test | erial \ | <u> </u> |
|------------------------------|-------------------|-------------------------------------|-------------|-----------------------------|-------------|----------|----------|
| NA Posi | tive Contro | l Group N | A Vehic | le <u>NA</u> | An: | | 6410- |
| | _ | 7 10/81 | | | Date | Initi | ated _ |
| Source De | an Da | ul Sex | <u></u> | • | Challe | enge D | ate _E |
| | .# | | | 1 | 2 | | |
| | | | | • | Technicia: | Recorded | Date |
| Sensi- tizing Dose No. | Dose ⁴ | Obser- vation Period (Hrs) | Erythema | Edema | cian | ded By | 1981 |
| | 0.4 | NA | NA | NA | çe. | ER | 7/22 |
| | | 24 | C | 0 | W | ۶۶ | 7 (23 |
| • | | 48. | 8 | 0 | | JR | 7/24 |
| · | 0.4 | NA | NA | NA | NOR | NER | 1 29 |
| a | | 24 | 0 | 0 | Sh | 120 | 7/30 |
| | | 48 | 0 | | 100 | 1000 | 73 |
| 3 | 0.4 | NA_ | NA | NA. | De | N. | 2/5 |
| 3 | | . 24 | Q· | Q | ADY | 1/20 | 216 |
| | | 48 | 0 | 0 | ER. | ER | 8]7 |
| Challenge | 0.4 | NA | NA. | NA | <u>ερ</u> _ | EP | 9/19 |
| Dose | | 24 | 0 | 2 | ا دو | da | 8/20 |
| | 1 | 48 | 0 | 0 | ER | des | 801 |

NA

24

a - Dosage applied by technician indicated
 NA - Not Applicable

| | | | A Vehicl | | lingMate | rial \ | Ariso 195 - 6410 - |
|------------------------------|---------------------------|-------------------------------------|-----------|---------|------------------|-------------------|--------------------------|
| | _ | 7/10/81 u/ Sex | <u>\$</u> | | | | ated 7 |
| | .# | | | | Cecho | Recorded | Date |
| Sensi- tizing Dose No. | Dose ² (ml) | Obser- vation Period (Hrs) | Erythema | Edema | echnician | rded By | 1981 |
| | 04 | NA 24 48 | NA C | NA C | de NAV | ER ER JK | 7 22 1 23 7774 |
| a | 0.4 | NA 24 48 | NA C | NA O | 100 100 | 100 are 101 | 7/30 7/31 |
| 3 | 0.4 | NA 24 48 | NA O | NA O | DA AXIV FR | NA ER | 85 80 81 |
| Challenge | 0.4 | NA 24 | NA D | NA O | 66 60 | ER | 8 19 3/20 |

0.5

NA

NA

48

24

a - Dosage applied by technician indicated
 NA - Not Applicable

| Der | mal | Sens: | itization : | In | Guinea | Pigs | _ | Body | Weight | s | | |
|-------|-----|-------|-------------|----|---------|---------------------|---|--------------|--------|----------|----------------------------|---|
| | | | | | | | | | | | Varisoft 475 | |
| Group | _RT | No. | 81160 | רי | Vehicle | 20.9 9 ₀ | 5 | <u>aline</u> | Test | Compound | Varisoff 475 Lot 195-13 | 6 |

| VA | Positive | Control | Group | NA | Vehicle | NA | |
|----|----------|---------|-------|----|---------|-----|--|
| | | | E | | | /∨~ | |

| | | | Animal | Number | | 1 | |
|-------|-------|--------------|--------|--------|---|-----------------|--------------|
| 6410- | 6410- | 6410- | 6410- | | | | |
| 0382 | 0398 | 0445 | 0446 | | • | Tech- nician | Date 1981 |
| 375 | 322 | 340 | 379 | | • | | , |
| | Jaa | 3 6 8 | | | | ER_ | 7 22 |
| 460 | 419 | 456 | 442 | | | صرم | 7/29 |
| 548 | 490 | 524 | 496 | | | JP | 8/5 |
| 604 | 551 | 595 | 532 | | | Ye. | glia |
| 692 | 601 | 651 | 566 | | | 23 | 8/19 |
| | | | | | | | |

| A | Animal Number | | |
|---|-------------------------|-----------------|------|
| | | Tech- nician | Date |
| | Scale Used: K.Tron 4809 | ER | 7/22 |
| | Scale Used: K-Tron 4809 | - pyo | 7/29 |
| | Scale Used: K-Tron 4809 | 180 | 8/5 |
| | Scale Used: KTRON 4809 | Sh | 8/12 |
| | Scale Used: KiTron 4809 | ER | 8/19 |
| | -\ - Scale Used: | | |

NA - Not Applicable

Oform change 7/22/81 ER

Dermal-Sensitization in Guinea Pigs - Daily Observations

| $\boxtimes_{\mathfrak{C}}$ | Naive Test Group | RT No. 8 | 11607 | vehicle 0.9 % saline | Test Com | √م pound لوا | risoft 4752 t 195-136 |
|----------------------------|---------------------|-----------|-------|----------------------|----------|-----------------|--------------------------|
| NA | Positive Con | atrol Gro | upNA | Vehicle M | A Roo | m No. | 2 |

| | | . An | imal Numb | er | • | | | 7 | |
|--------------------|--------|---------------------|--------------------|----|---|---|---|-----------------|--------------|
| 6410- 0382 T | 0398 | 6410 - 0445 9 | 6410- 0446 9 | | | · | | Tech- nician | Date 1981 |
| N | N | Ν | Ν | | | | | E.C. | בגוד |
| N | N | Ν | N | | | | | ER | 7/23 |
| N | N | N | N | | | | | JL | 7/24 |
| N | N | N | N | · | | | | R | 725 |
| | N | Ν | \mathcal{N} | | | | | JR | 7/26 |
| N | N | Ν | N | | | | | IK | 7/27 |
| N | N | N | N | | | | | NON | 7/28 |
| N | N | N | N | | | | , | NJI | 7/29 |
| 2 | \sim | N | , N | | | | | dh | 7/30 |
| 2 | N | N | ν. | | | | | gg | 7/3/ |
| 2 | 2 | 2 | N | | | | Š | rys | 8/1 |
| 2 | 2 | <u> </u> | \sim | | | | | chit. | 8/2 |
| 2 | \sim | ر ۸ | \mathcal{N} | | | | | del | 8/3 |
| N | \sim | N | N | | | \ | \ | CS | 8/4 |
| N | N | N | N | | | | | R | 8/5 |
| N | _ N_ | N | V | | | | | NOO | Alco |
| N | N | N | N | | | | | ER. | 8/7 |
| Oform | N | 7/20/81 | $ \mathcal{N} $ | · | | • | V | \mathcal{R} | 3/9 |

Oform change 7/20/81 ER

N - No Visible Abnormalities

NA - Not Applicable

| ⊠ _O | <u>Dermal</u> ive | -Sensitiz RT No. | <u>ation in</u> 871607 | Guinea Pi | igs - Daii sterile 2990 salir | ly Observ | etions | Varis oft | 475 : |
|-----------------------|----------------------|---------------------|-------------------------------|-----------|-------------------------------------|-----------|------------|----------------------|--------------|
| NA Po | ositive C | ontrol Gr | onb N | A Veh | dcle/ | VA B | oom No. | 2 | |
| | | An | imal Numb | er | | | | | |
| 6410- 03 83 | | 6410 - 0445 9 | 6410- 0446 Q | | | · | | Tech- nician | Date |
| N | N | N | N | | | | | SP | 8/9 |
| 2 | 7 | 7) | N | | | | | day | 8/10 |
| N | N | N | N. | | | | | JR | 8/11 |
| N | N | N | Ŋ | | \ | | | DR | 8/13 |
| N | \mathcal{N} | N | | | | | <u> </u> . | ER | 8/13 |
| N | N | N | \mathcal{N} | | \ . | | | des | 8/14 |
| | N | . 7. | \ | | 1 | | | <u> </u> | 8/15 |
| N | <i>N</i> . | N | N | | | | | doto | 8/16 |
| N | Ν | N | N | | | \ | | dou | 8/17 |
| N | ~~ | N | N | | | | | Sc | 8/18 |
| N | N | N | Ŋ | | | | š | ER | 8/19 |
| N | N . | N | N | | • | | | da | 8/20 |
| N | <i>ν</i> | N | N | | | | | dev | 8/2/ |
| ₩- | -N- | ~ | | | | | <u> </u> | HOLD) | 8/02 |
| · | - | _ | . : | | | | \ <u> </u> | • | |

Oform change 7/20/81 ER

N - No Visible Abnormalities

NA - Not Applicable

2) RECORDING 8/17/8/ 20

Naive Fess Group: sterile Test

Varisoft 475 RT No. 871607 Venicle 0990 saline Material Lot 195-136

7/10/81 Date Animal Received _ Date Initiated 7/22/81 Sex 3 9 Source Dean Daul Challenge Date 8/19/81 Obser-Edeme Dose⁴ Erythess animal No. vacion Period 6410-1981 (Hrs) 0.4 <u> 18 19</u> 0382 1.0% 0.4 0398 8 19 NA NA NA das 8/20 24 0 1.090 0.4 0445 e 8/19 NA 1.0% de) 881 0.4 0446 8/19 NA 9 24 1.0% (de) 8/21 48 0 NA AK 24

⁻ Dosage applied by technician indicated

NA - Not Applicable Oform change 7/21/81 ER

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Test Group:

RT No. 871607 Vehicle Sterile 0.99 Material Varisoft 475: Saline Lot 195-136

Date Animal Received 5/28/81

Source Dean Daul Sex 3 Date Initiated 7/9/81

| | | | · | · | Tech | Reco | D ₂ |
|------------|------------------------|--------------------------------|-----------|------------|--------------|--|---|
| 6410 - | Dose ² (ml) | Observation Period (Hrs) | Erytheme. | Edema | nician | Recorded by | Mate //98 / |
| ~ - | 0.5 | NA | NA. | NA | ER. | se. | 719 |
| 0295 | 100 | 24 | 0 | 0 | KTX | 1 66 | 7/10 |
| | | 48 | 1 0 | | MP | NR | 7/) |
| ر س م | 0.5 5.0% | na | NA | N A | È R . | SR | 7/9 |
| 0245 | 5 x 01. L | 24 | 1.0 | 1.0 | MA | e. | 7/10 |
| (B) | 3.0 701 | 48 | 1-0 | 0 | Me | W. | 711 |
| | | Na | NA | · NA | | į | |
| | | 24 | | | | | - |
| | 7 | 48 | | | | : | |
| | | NA | NA | NA | | ļ | |
| • | | 24 | | ı İ | ٠, | | ! |
| | | 48 | | | | د آ | <u> . </u> |
| | | NA | 7A | NA | | : | |
| | | 24 | | | | | |
| | | 48 | | İ | | <u>. </u> | |

a - Dosage_applied by technician indicated

NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Test Group:

RT No. 871607 Vehicle Sterile 0.9% Material Varisoft 475: Saline Lot 195-136

Source Dean Daul Sex 6 Date Initiated 7981

| 410 - | Dose ² (ml) | Obser- vation Period (Hrs) | Erythema | | Technician | Recorded by | 1981 |
|-----------|------------------------|-------------------------------------|-----------------|--------|------------|-------------|------|
| . 0.70 | 0.5 | NA | HA | NA | جع. | 50 | 7/9 |
| 0272 A | 5.0% | 24 48 | ن ا 0 | 0 | MR | 1 EP | 7110 |
| | 0.5 | NA | AK | NA | ER | | 17/9 |
| 0272 | 1.0% | 24 48 | 0 | 6 | MP | ER | |
| | | NA | NA | · NA | | ì | / |
| | | 24 | | l i | | : | |
| | | KA | NA | NA | • | | |
| | | 24 48 | | 1 | 1 | ; ! | l . |
| | | MA | ÄĀ | NA | 1 | ! | |
| | | 24 48 | | | | | |

a - Dosage applied by technician indicated

NA - Not Applicable

|) acc | | <u></u> | |
|------------------|------------------------|---|---------------------|
| | | STUDY IN GUINEA PIGS | |
| Test Group: | RT No. <u>87/607</u> v | Sterile 0.9% Test Venicle Variof 7 Mater | ial Varisoft + |
| Date Animal Rece | ived 4/10/81 | Saline Date Initia | ced <u>6/22/8</u>) |
| | | | 7 |

| WHIO- LIMEL NO. SITE | Dose ² (m/) | Obser- vation Period (Rrs) | Erythess | Edess | rechnicien | Recorded by | 1981 |
|----------------------------|---------------------------|-------------------------------------|------------|---------|--------------------------|-------------|-------|
| 0179 (A) | 0.5 | NA 24 | NA 2, C | NA /. O | NOO | | 10/22 |
| 0179 | 25% | 4.8 NA | 2. C) | 2. O | NCN | V35 | 6/22 |
| (B) | 50% | 24 | 7.0 | 2.6 | | NOA | 6/23 |
| 0/79 | 0.5 | NA 24 48 | 2. O | 1. U | W.DV W.DV W.DV | NDO | 10/23 |
| 0179 | 0.5 | NA | NA | NA | NO | NDO | 10/22 |
| (3) | 100% | 24 48 | 2.0 | 1.6 | 1300 VW | 109 | 624 |
| | | 74 24 48 | AV. | NA | | | |

a - Dosage applied by technician indicated
 NA - Not Applicable

O Recording Error 6/22/81 NOA

Head

Dose Range

| | DEI | RMAL SENSITIZA | TION STUDY IN | GUINEA PIO | <u>ss</u> | | |
|---------------|-------------|------------------|--------------------|------------|-----------------|-------------|--------|
| Test Gro | oup: Ri | No. <u>87/6</u> | <u>O</u> 7venicle∫ | torile 0,9 | Test Materia | 1 Var | isoft |
| | | | • | Saline | • | 19 | 5-130 |
| | | | | • | | | |
| Date Anim | AL RECEIVED | 4/10/ | 7 | . | | . , | 10-10 |
| Source | Dean 1 | Daw ! | iex | Da Ca | Initiate | d <u>@/</u> | 22/8 |
| | • | | | | | _ | |
| | | | | | [ec | Rec | |
| 1 1/10 = | | | | | [eclmiciar | Recorded | Date |
| 6410 - | Dose | Obser- vation | Erythema | Edema | Lar | e | |
| (5/te) | (mi) | Period | | | | 87 | 1981 |
| \ | | (Hrs) | | | 1 . 700 | 100.4 | |
| 0160 | 0,0 | NA | NA | . NA | 1 1/000 | NXX | 6/22 |
| Θ | 100% | 24 48 | 2.0 | 120 | CCCA | 1772 | 624 |
| 0140 | 0.5 | | NA. | NA. | 1/70 | NOO | 10/22 |
| B | | NA 24 | 2.0 | 1.0 | DC.NI | VIDA | D/23 |
| 0 | 25% | 48 | 2.0 | 2.0 | 1127 | 101 | 10124 |
| 0160 | 05 | · • NA | - NA | · NA | 200 | NO | 10/22 |
| | 50% | 24 | 2.0 | 11.0 | INON | NON | h/73 |
| | 3070 | 48 | 2.0 | 120 | 1027 | 112 | 10124 |
| 0/60 | 0.5 | NA | NA | NA | 1000 | NOV | 6/22 |
| (D) | 157 | 24 | 2.0 | 1.0 | IVO | | 10123 |
| | 75% | 4.8 | 2.0 | · Z. O | 1721 | 100 | 1 1957 |
| | | *** | A.K. | NA | | ! | |
| | | 24 | | | | i . | i |
| | Ţ | 48 | | | | 1 | |

a - Dosage applied by technician indicated
 NA - Not Applicable

Tail

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Test Group:

) 99 Test) 99 Material VariSoft 475

Date Initiated 6/22/8

| | | | · | | [ec] | Rec |
|----------------------------------|-------------------|-------------------------------------|--------------|-------------------|--------------|------------|
| (0410 - lacimal No. (Site) | Dose ² | Obser- vation Period (Hrs) | Erythems. | · Edema | nician | Date 198 |
| 034 | 0.5 | NA | NA | NA | NOX | NON 6/22 |
| | 75% | 24 48 | 2.0 | 1 2.0 1 z.0 | MX | 11/20/0/23 |
| 0136 | 0.5 | MA | NA | NA. | NO | NOO! 6/22 |
| 8 | 100% | 24 48 | 7.0 | 2.0 | NOX NOX | ND0 6/23 |
| 0136 | 05 | . NA | NA | · NA | NEW | NON 6/22 |
| | 25% | 24 | 1. O 2. O | 1 G 1 Z. O | WILL PELL | NON 10/23 |
| 0136 | 0.5 | NA | NA | NA | NOO | NO 6/22 |
| (D) | 50% | 24 I | 2.0 2.0 | · Z. C/ · Z. O | NOV I | ESTATION: |
| | | 114 | . YA | NA | | |
| | | 24 48 | | | | |

a - Dosage applied by technician indicated

NA - Not Applicable



| Yest Group: | RT No. 871100 | 07 Veni | el Stonile 0.9% Material | Varisoft - |
|-----------------|----------------|---------|--------------------------|------------|
| | | | Saline | 195-13 |
| Date Animal Rec | ceived _ 4/10/ | 81 | | |
| Source De | on Daul | Sex | C Date Initiated | 6/22/81 |

| LO410- Lacimal No. Site | Dose ² | Obser- vation Period (Hrs) | Erytheme. | Edeme. | Technician | Date 9 |
|-------------------------------|-------------------|-------------------------------------|--------------|--------------|------------|--------------------|
| 0189 | 0.5 | KA | NA | NA | NOS | NOR 10/2 |
| (A) | 50% | 24 48 | 2.0 | Z.O Z.Q | N.X | 11/10 b/23 |
| 0/89 | 05 | NA | MA | NA | NN | NO 6/22 |
| (3) | 75% | 24 | 2 O 2. O | 12.0 12.0 | VOX | NX 6/23 |
| 0189 | 0.5 | . NA | NA | · NA | NOO | NDO 6/22 |
| 0 | 100% 1 | 24 48 | 5.0 5.0 | 12.0 | INDX | NN 5/23 |
| 0/89 | 0.5 | NA | NA | NA | NOO | ND9 16/22 |
| | 25% | 24 | 7. O 2. O | · 0 | I NOO | 150 16123 10123 |
| | | WA | NA. | NA | | |
| | | · 24 | | | | |

a - Dosage applied by technician indicated
 NA - Not Applicable

Head B/B Tail

Dose Range

| | oup: F | RT No. 87/100 | <u>77</u> Venicle 57 | GUINEA PI Ler, le 0.9% Saline | Test Materi | a1 <u>Va</u> | urisof F/13 |
|-------------------|-------------------|--------------------------|----------------------|-------------------------------------|--------------------|--------------|----------------|
| | | Daul | | Date | Initiat e | 1 | 12218 |
| Animal No. (Site) | Dose ⁴ | Observation Period (Hrs) | Erythema | Edema | <u> Tecimician</u> | Recorded By | Date 1981 |
| 0192 | 0.5 | NA | NA | AN | NON | NOW | 6/2 |
| 9 | 10% | 24 | 1.0 | 0 | ACO | DCTVI | 10/23 |
| 0/92 | 0.5 | NA | NA. | NA | NON | 1 | 6/27 |
| 8 | 1070 | 24 | 10 | 1 9 | N179 | NOV | 10/23 |
| | | NA | NA | · NA | 1.30 | <u> </u> | - |
| | | 48 | | | 1 | ; | |
| | | NA | NA | NA. | | | |
| | | 24 1 | | i | | , | |
| | | NA 24 | NA | NA | | | |

a - Dosage applied by technician indicated NA - Not Applicable

48

• . ----

Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

Attachment 7:

Laboratory Report - Biodegradability [IQAC 68122-86-1]

LABORATORY REPORT

Test:

Biodegradability

Sample: Varisoft 475

Lab Data:

BOD₂₀ BOD_ 53,000 329,000 BOD₁₀ 286,000 BOD₃₀ 416,000

COD (analytical) 2,171,280 mg/L COD (theoretical) 2,220,000 mg/L

BOD₅/COD 0.02 BOD₂₀/COD 0.15 BOD₁₀/COD 0.13 BOD₃₀/COD 0.19

Reaction Rate Constant 0.07

Results: Based on the above data, we feel Varisoft 475 can be

considered biodegradable.

Analytical Procedures:

In determining the biodegradability of Varisoft 475, our laboratory conducted an Ultimate Oxygen Demand (UOD) study.

The product was aerated for eight (8) weeks with organisms supplied in settled raw sewage to acclimate them to this particular source of food. This was used as our seed material. In the UOD determinations, aliquots were incubated in the presence of the seed material at 20°C. Samples were taken ten (10) consecutive days and also after twenty (20) and thirty (30) days of incubation. BODs were determined on these samples (see _ attached analyses report), plotted against time and a reaction rate constant calculated.

COD: Chemical Oxygen Demand is determined by refluxing samples in 50% sulfuric acid solution with potassium dichromate which is the oxidizing agent. The amount of K2Cr20, required to oxidize the sample is the COD.

Director of Laboratory

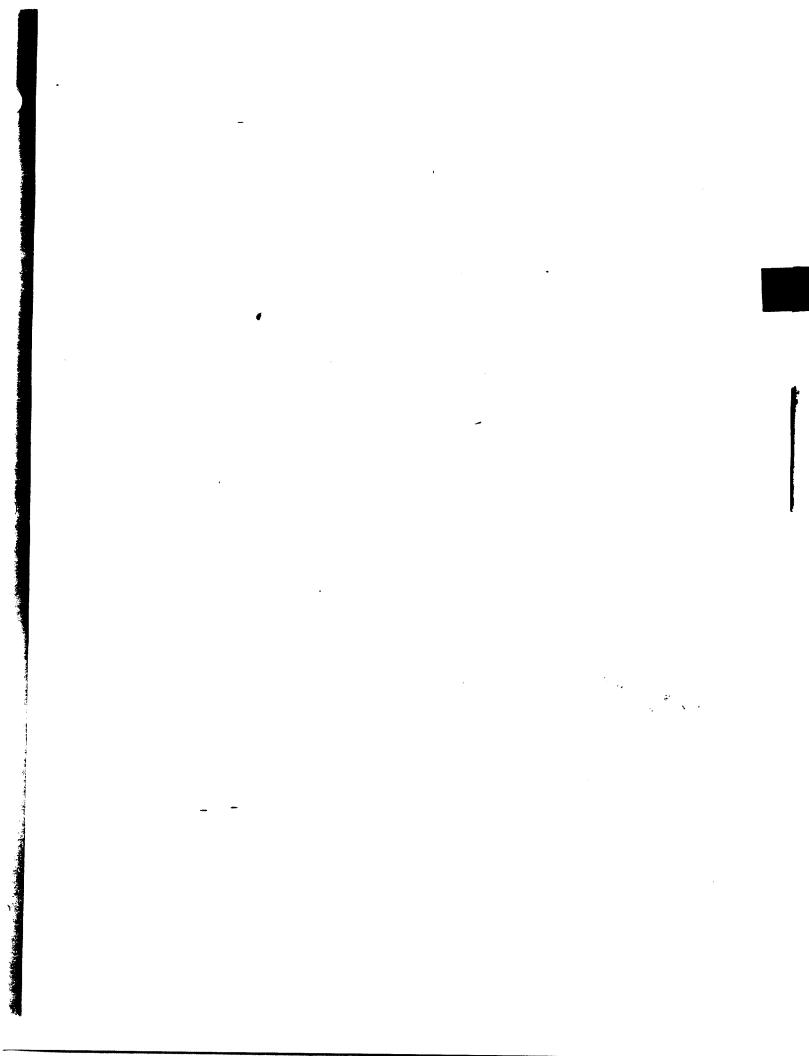


senco riydro/ Aerosciences, inc. (Chemical and Er issing Laboratory)

ANALYSIS REPORT

产

Ref. No. 3157 June 11, 1971 Director of Laboratory 8 30 Cartified by: Dele 329 8 20 286 8 10 336 8 9 119 800 Unless otherwise nated - results in milligram per liter (mgr1) œ BOD 120 65.0 **B**00 9 53.0 ₩. 42.0 202 **800** 28.0 28.0 17 ~ Northern Petrochemical Company 22.8 **B**00 2200 East Devon Avenue Des Plaines, Illinois Attn: Dr. H. Sanders Rosults in g/L Varisoft 475 Description 8549 Form A141-RI 7 Remarks **કે** કે P.3/4 MAE0:E0 <u>86.</u>



Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

Attachment 8:

WARF Institute Reports 8040871 & 8040872 - Skin Irritation, Eye Irritation, Acute Oral Toxicity [PEQ 68410-69-5]

MADISON, WISCONSIN

Reports are submitted to clients on a confidential basis. No reference to the work, the results or to the Institute in any f of advertising, news release or other public announcement may be made without written authorization from the Instit

REPORT

Primary Skin Irritation, Primary Eye Irritation,

Analysis for

Acute Oral Toxicity

Description of Sample

Date Received

3-31-78

Reference Number

Sample Code 211-58A

3/31/78

Submitted by

Ashland Chemical Company

Janesville, WI

Richard M. Egan

VARISOFF 22-96

Claimed Content

Results

Acute Oral LD50:

In excess of 5.0 grams per kilograms

of body weight.

Skin irritation index:

5.1

Eye Irritation score:

24 hr

Method

See attached protocols.

Remarks

In accordance with FHSA regulations, this product is not toxic orally, is irritating to the skin and is irritating to the eyes.

Date

May 11, 1978

WARF Institute No.

8040871

ACUTE ORAL TOXICITY

Client: Ashland Chemical Company

WARF Institute No.: 8040871

Sample: Code 211-58A

Test Animal: Male young adult albino rats (approximately 7 weeks of age) of the Sprague Dawley strain* were procured, maintained in group cages in air conditioned quarters, provided continuous access to commercial laboratory feed and water and held for a conditioning period of at least 7 days.

Method: Animals were chosen at random from the conditioned animals, dosed as specified and maintained individually in screen bottom cages with continuous access to feed and water for a two week observation period. Observations were made at hourly intervals for 5 hours after dosing and twice daily for the remainder of the two week period. At termination, surviving animals were sacrificed. Gross post mortem examinations were performed on all animals on test and gross tissue alterations noted.

Method of Administration: Stomach tubed.

Concentration of Test Material: As submitted.

Results:

| Dosage Level [1] (gm/kg) | | erage ghts (gma) Terminal | Mortality Number [2] Day [3] | | |
|--------------------------|-----|---------------------------------|------------------------------|---|--|
| 5.0 | 200 | 303 | 0/10 | - | |

Oral LD50: In excess of 5.0 grams per kilogram of body weight.

- [1] Of test material
- [2] Number dead/number dosed
- [3] Period during which deaths were observed

Other Observations: Necropsies were done on all of the animals.

None of the animals had any remarkable tissue

alterations.

^{*} ARS/Sprague Dawley - Madison, Wisconsin



MADISON, WISCONSIN

PRIMARY SKIN IRRITATION

Client Ashland Chemical Company

WARF Institute No. 8040871

Sample Code 211-58A

Test Animal: Young adult rabbits (approximately 14 weeks of age) of the New Zealand white strain weighing 2.5 to 3.5 kg were procured, maintained individually in screen bottom cages in air conditioned quarters, provided continuous access to commercial laboratory feed and water and held for a conditioning period of at least 7 days.

Method: Conditioned animals were chosen at random, treated and maintained as specified for the conditioning period.

The hair was clipped from the back and flanks of the animal. The test material was applied to two areas on each rabbit, I abraded area, and I intact area, in the amount of 0.5 ml per area in the case of liquids or 0.5 gm per area in the case of solids. The treated areas were covered with a gauze patch and taped to maintain the test material in contact with the skin and decrease the rate of evaporation. The animals were immobilized for a 24 hour period at which time the coverings were removed and the degree of crythema and edema were recorded according to the scale below. A second reading was taken at 72 hours. The average of the 24 and 72 hour readings were used to determine the primary irritation index for the sample.

Concentration of Test Material: as submitted

Results:

| | | 24 Ho | urs (| L) | 72 Hours (1) | | | |
|------------------|--------------------|-------|----------------------|----|--------------------|------|----------------------|---|
| Animal Number | Abraded Er. Ed. | | Unabraded Er. Ed. | | Abraded Er. Ed. | | Unabraded Er. Ed. | |
| 196 | 3 | 2 | 3 | 2 | 3 | 2 | 3 | 2 |
| 197 | 3 | 2 | 3 | 2 | 3 | 2 | 3 | 2 |
| 198 | 3 | 2 | 3 | 2 | 3 | 3 | 3 | 3 |
| 199 | 3 | 2 | 3 | 2 | 3 | 2 | 3 | 2 |
| 200 | 3 | 2 | 3 | 2 | 3 | 2 | 3 | 2 |
| 201 | 3 | 2 | 3 | 2 | 3 | 2 | 3 | 2 |
| Score | 24- | hour | 5.0 |) | 72- | hour | 5.2 | 2 |

Primary Skin Irritation Index (2): 5.1

(1) Score equals sum of erythems and edems readings.

(2) Skin irritation index equals average of 24 and 72 hour scores.

| Erythema and Eschar Formation | Score | Edema Formation | Score |
|-------------------------------|-------|----------------------|-------|
| Slight erythema | 1 | Slight edema (barely | |
| Defined erythema | 2 | perceptible) | 1 |
| Moderate to severe erythema | 3 | Defined edema (edges | _ |
| Severe erythema to slight | | definite rising) | 2 |
| eschar formation | 4 | Moderate edema (area | |
| | | raised 1 mm) | 3 |
| | | Severe edema (raised | |
| | | more than 1 mm) | 4 |

EYE IRRITATION Client: Ashland Chemical Company

WARF Institute No.: 8040871 Sample: Code 211-58A

Test Animal: Young adult rabbits (approximately 14 weeks of age) of the New Zealand white strain weighing 2.5 to 3.5 kg were procured, maintained individually in screen bottom cages in air conditioned quarters, provided continuous access to commercial laboratory feed and water and held for a conditioning period of at least 7 days.

Method: Conditioned animals were chosen at random, treated and maintained as specified for the conditioning period.

For each animal treated, one-tenth of a milliliter (0.1 gm for solids) of the test substance was instilled into one eye and the untreated eye served as a control. The reaction to the test material was read according to the scale of scoring for damage at specified times after instillation. Any residue of the test material and accumulated discharge were flushed from the eyes each time they were scored.

Concentration of Test Sample: As submitted.

Special Washing: None

Results:

| | Rabbit | Cornea | | | Conjunctivae | | | |
|---------|------------------|--------|-------|------|--------------|---------|----------|-----------------|
| | Number | Ор | acity | Area | <u>Iris</u> | Redness | Chemosis | Discharge |
| | 259 | | . 0 | 0 | 0 | 2 | 0 | 0 |
| | 260 | | 0 | 0 | 0 | 0 | Ō | Ō |
| | 261 | | 0 | 0 | 0 | 2 | 1 | 1 |
| 24 Hour | 262 | | 0 | 0 | 0 | 1 | 0 | 0 |
| | 263 | (d) | 1 | 4 | 1 | 2 | 3 | 0 3 . |
| | 264 | , | 0 | 0 | 0 | 2 | 2 | 1 |
| | | | | | | | | |
| | | | | Eye | Irritation | Score: | 10.8 | #** *** |
| | 259 | | 0 | 0 | 0 | 2 | 0 | 0 |
| | 260 | | 0 | 0 | 0 | 0 | 0 | 0 |
| | 261 | | 0 | 0 | 0 | 1 | 0 | 1 |
| 48 Hour | 262 | | 0 | 0 | 0 | 0 | 0 | 0 |
| | 263 | (b) | 1 | 4 | 1 | 2 | 2 | 3 |
| | ⁻ 264 | | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | | Eye | Irritation | Score: | 8.2 | |
| | | | _ | _ | _ | _ | _ | |
| | 259 | | 0 | 0 | 0 | 0 | 0 | 0. |
| | 260 | | 0 | 0 | 0 | 0 | 0 | 0 |
| 70 | 261 | | 0 | 0 | 0 | 0 | 0 | 0 |
| 72 Hour | 262 | | 0 | 0 | 0 | 0 | 0 | 0 |
| | 263 | (b) | 1 | 4 | 1 | 2 | 3 | 3 |
| | 264 | | 0 | 0 | 0 | 0 | 0 | 0 |

Eye Irritation Score: 6.8

EYE IRRITATION (Continued)

Client: Ashland Chemical Company

WARF Institute No.: 8040871

Sample: Code 211-58A

Results:

| | Rabbit | Corn | ea | | | Conjunctiv | ae |
|-------|--------|----------------|------|------|---------|------------|-----------|
| | Number | <u>Opacity</u> | Area | Iris | Redness | Chemosis | Discharge |
| | 259 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 260 | 0 | 0 | 0 | Õ | Ö | Ö |
| | 261 🖣 | 0 | 0 | 0 | Õ | Ö | Õ |
| Day 7 | 7 262 | 0 | 0 | 0 | 0 | Ō | ő |
| | 263 | (b) 2 | 3 | 0 | 2 | 2 | i |
| | 264 | 0 | 0 | 0 | 0 | 0 | ō |

Eye irritation score: 6.7

FORM 28-4

⁽b) Sloughing of 25-49% of the corneal epithelium.

⁽d) Sloughing of 75-100% of the corneal epithelium.

eports are submitted to clients on a confidential basis. No reference to the work, the results or to the Institute in any form f advertising, news release or other public announcement may be made without written authorization from the Institute.

REPORT

Primary Skin Irritation, Primary Eye Irritation,

Analysis for

Acute Oral Toxicity

Description of Sample Varisoft 222-90%

Date Received

3-31-78

Reference Number

Sample Code 211-58B

Submitted by

Ashland Chemical Company

Janesville, WI

Richard M. Egan

JARISOFT 222-90

Claimed Content

Results

Acute Oral LD50:

In excess of 5.0 grams per kilogram

of body weight.

Skin irritation index:

5.2

Eye Irritation score:

Method

See attached protocols.

Remarks

In accordance with FHSA regulations, this product is not toxic orally, is irritating to the skin and is irritating to the eyes.

by and for the WARF INSTITUTE, INC.

Date

May 11, 1978

WARF Institute No.

3040872

ACUTE ORAL TOXICITY

Client: Ashland Chemical Company

WARF Institute No.: 8040872

Sample: Code 211-58B

Test Animal: Male young adult albino rats (approximately 7 weeks of age) of the Sprague Dawley strain* were procured, maintained in group cages in air conditioned quarters, provided continuous access to commercial laboratory feed and water and held for a conditioning period of at least 7 days.

Method: Animals were chosen at random from the conditioned animals, dosed as specified and maintained individually in screen bottom cages with continuous access to feed and water for a two week observation period. Observations were made at hourly intervals for 5 hours after dosing and twice daily for the remainder of the two week period. At termination, surviving animals were sacrificed. Gross post mortem examinations were performed on all animals on test and gross tissue alterations noted.

Method of Administration: Stomach tubed.

Concentration of Test Material: As submitted.

Results:

| Dosage Level [1] (gm/kg) | Aver Body Weigh Initial | ts (gms) Terminal | Mortal: Number [2] | ity Day [3] |
|--------------------------|-------------------------------|----------------------|----------------------------------|----------------|
| 5.0 | 220 | 310 | 0/10 | - |
| | Oral LD ₅₀ | | ss of 5.0 grams of body weigh | per « |

- [1] Of test material
- [2] Number dead/number dosed
- [3] Period during which deaths were observed

Other Observations: Necropsies were done on all of the animals. One of the animals showed atrophy of the right testicle. None of the remaining animals showed any remarkable tissue alterations.

^{*} ARS/Sprague Dawley - Madison, Wisconsin

WARF INSTITUTE, INC.

MADISON, WISCONSIN

PRIMARY SKIN IRRITATION

Client: Ashland Chemical Company

WARF Institute No.: 8040872

Sample: Code 211-58B

Test Animal: Young adult rabbits (approximately 14 weeks of age) of the New Zealand white strain weighing 2.5 to 3.5 kg were procured, maintained individually in screen bottom cages in air conditioned quarters, provided continuous access to commercial laboratory feed and water and held for a conditioning period of at least 7 days.

Method: Conditioned animals were chosen at random, treated and maintained as specified for the conditioning period.

The hair was clipped from the back and flanks of the animal. The test material was applied to two areas on each rabbit, I abraded area, and I intact area, in the amount of 0.5 ml per area in the case of liquids or 0.5 gm per area in the case of solids. The treated areas were covered with a gause patch and taped to maintain the test material in contact with the skin and decrease the rate of evaporation. The animals were immebilized for a 24 hour period at which time the coverings were removed and the degree of crytheum and edems were recorded according to the scale below. A second reading was taken at 72 hours. The average of the 24 and 72 hour readings were used to determine the primary irritation index for the sample.

Concentration of Test Material: As submitted.

Results:

| | | | Hours (1) | | | 72 Hours (1) | | | |
|--------|------|------------|-----------|------|------|--------------|-----|-------|--|
| Animal | Abra | | Unabr | aded | Abra | | | raded | |
| Number | Er. | <u>Ed.</u> | Er. | Ed. | Er. | Ed. | Er. | Ed. | |
| 196 | 3 | 2 | 3 | 2 | 3 | 3 | 3 | 3 | |
| 197 | 3 | 2 | 3 | 2 | 3 | 2 | . 3 | 2 | |
| 198 | 3 | 2 | 3 | 2 | 3 | 2 | 3 | 2 | |
| 199 | 3 | 2 | 3 | 2 | 3 | 2 | 3 | · 2 | |
| 200 | 3 | 2 | 3 | 2 | 3 | 3 | 3 | 3 | |
| 201 | 3 | 2 | 3 | 2 | 3 | 2 | 3 | 2 | |
| Score | 24-b | ur | 5.0 | | | 72-t | our | 5.3 | |

Primary Skin Irritation Index (2): 5.2

- (1) Score equals sum of erythems and edems readings.

(2) Skin irritation index equals average of 24 and 72 hour scores.

| Erythema and Eschar Formation | Score | Edema Formation | Saara |
|-------------------------------|-------|-----------------------|-------|
| Slight erythems | 1 | Slight edema (barely | Score |
| Defined erythema | 2 | perceptible) | 1 |
| Moderate to severe erythema | 3 | Defined edema (edges | _ |
| Severe erythems to slight | | definite rising) | 2 |
| eschar formation | 4 | Moderate edema (area | |
| | | raised 1 mm) | 3 |
| | | Severe edemn (raised) | |
| | | more than 1 | 4 |

WARF INSTITUTE, INC.

MADISON, WISCONSIN

EYE IRRITATION

Client: Ashland Chemical Company

WARF Institute No.: 8040872

Sample: Code 211-58B

Test Animal: Young adult rabbits (approximately 14 weeks of age) of the New Zealand white strain weighing 2.5 to 3.5 kg were procured, maintained individually in screen bottom cages in air conditioned quarters, provided continuous access to commercial laboratory feed and water and held for a conditioning period of at least 7 days.

Method: Conditioned animals were chosen at random, treated and maintained as specified for the conditioning period.

For each animal treated, one-tenth of a milliliter (0.1 gm for solids) of the test substance was instilled into one eye and the untreated eye served as a control. The reaction to the test material was read according to the scale of scoring for damage at specified times after instillation. Any residue of the test material and accumulated discharge were flushed from the eyes each time they were scored.

Concentration of Test Sample: As submitted

Special Washing: None

Results:

| | Rabbit | Corne | 04 | | (| onjunctiva | • |
|---------|------------|---------|------|------------|----------|------------|-----------|
| | Number | Opacity | Area | Iris | Redness | Chemosis | Discharge |
| | 283 | 1 | 4 | 0 | 2 | 3 | 3 |
| | 284 | 0 | Ó | Ö | 2 | 1 | 2 2 |
| | 285 | 0 | ŏ | ŏ | 0. | 1 | |
| 24 Hour | 286 | Ō | ŏ | ŏ | 2 | 0 | 0 |
| | 287 | Ō | ŏ | ő | 7 | 1 T | Ţ · |
| | 288 | Ŏ | Ŏ | Ö | 2 | 2 | 0 1 |
| | | | Eye | Irritation | n Score: | 11.0 | |
| | 283 | 1 | 1 | 0 | 2 | 2 | |
| | 284 | 0 | 0 | Ŏ | ō | Ō | Ŏ |
| | 285 | Ö | Ŏ | ŏ | ŏ | o . | Ţ., |
| 48 Hour | 286 | Ö | Ŏ | ŏ | 1 | 0 | 0 |
| | 287 | 0 | Õ | ŏ | î | • | • |
| | 288 | Ō | Ö | ŏ | Ō | 0 | 0 |
| - | | | Eye | Irritation | Score: | 3.5 | |
| | | | • | | | | |
| | 283 | 1 | 1 | 0 | 0 | 0 | 0 |
| | 284 | 0 | 0 | 0 | Õ | Õ | ŏ |
| | 285 | 0 | 0 | Ö | Ö | ŏ | ő |
| 72 Hour | 286 | 0 | 0 | Ö | Ö | ŏ | Ŏ |
| | 287 | 0 | 0 | Ö | Ö | Õ | ŏ |
| | 288 | 0 | ō | 0 | ő | Ŏ | Ö |

Eye Irritation Score: 0.8

EYE IRRITATION (Continued)

Client: Ashland Chemical Company

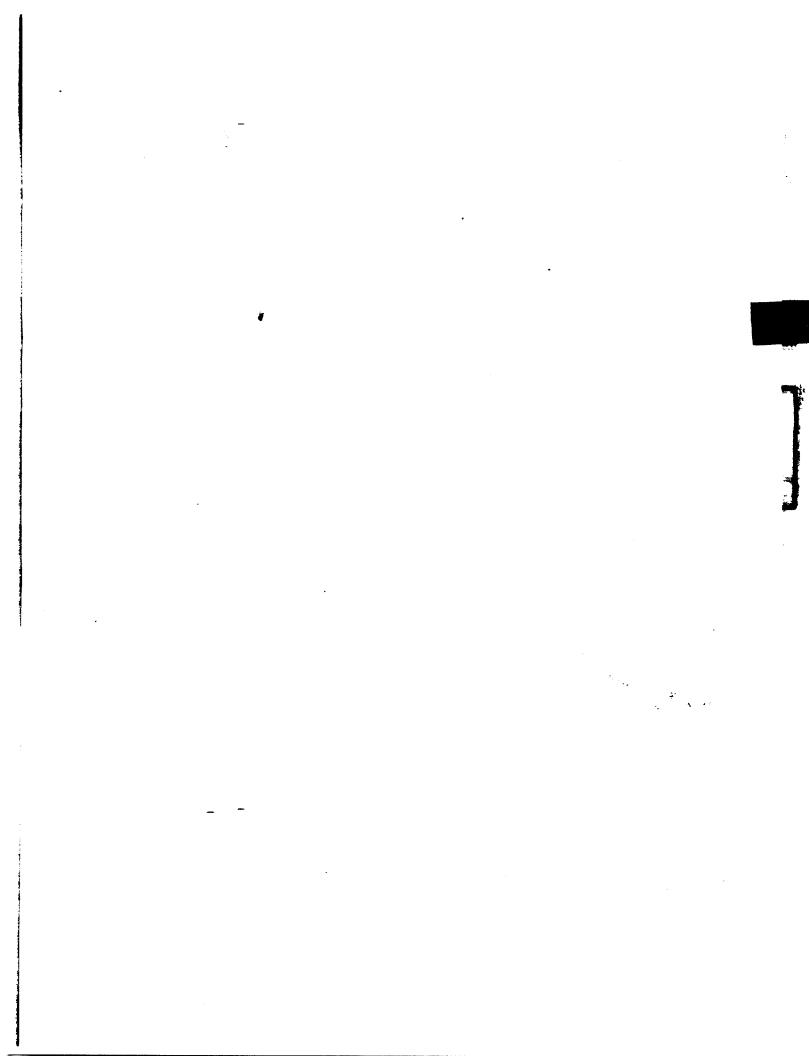
WARF Institute No.: 8040872

Sample: Code 211-58B

Results:

| | 1 | Rabbit | | Corn | 22 | | | Conjunctiv | æe |
|-----|---|--------|----------|---------|------|------|---------|------------|-----------|
| | 1 | Numbe | <u>T</u> | Opacity | Area | Iris | Redness | Chemosis | Discharge |
| | | 283 | | 1 | 1 | 0 | 0 | 0 | 0 |
| | | 284 | | 0 | 0 | 0 | 0 | 0 | Ö |
| | | 285 | • | 0 | 0 | 0 | 0 | 0 | 0 |
| Day | 7 | 286 | | 0 | 0 | 0 | 0 | 0 | 0 |
| | | 287 | | 0 | 0 | 0 | 0 | . 0 | 0 |
| | | 288 | | 0 | 0 | 0 | 0 | 0 | 0 |

Bye irritation score: 0.8



Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

Attachment 9:

WARF Institute Reports 8040875 & 8040876 - Skin Irritation, Eye Irritation, Acute Oral Toxicity [PEQ 68410-69-5, 5% dispersion]

Reports are submitted to clients on a confidential basis. No reference to the work, the results or to the Institute in any of advertising, news release or other public announcement may be made without written authorization from the Ins

REPORT

Analysis for

Primary Skin Irritation, Primary Eye Irritation, Acute Oral Toxicity

Description of Sample

Date Received

3-31-78

Reference Number

211-58E

3/30/78

Submitted by

Ashland Chemical Company

Janesville, WI

Richard M. Egan

5% DISPERSION OF 222-90 LOT 211-58A

Claimed Content

Results

Acute Oral LD50: in excess of 5.0 grams per kilogram of body weight

Skin Irritation Index:

0.8

Eye Irritation Scores:

24 Hr.

Method

Please see the attached protocols.

Remarks

shewing

In accordance with FHSA regulations, this product is not toxic orally, is not irritating to the skin, and is not irritating to the eyes.

Signed Jeusen

by and for the WARF INSTITUTE. INC.

Date

May 11, 1978

WARF Institute No.

8040875

ACUTE ORAL TOXICITY

Client Ashland Chemical Company

WARF Institute No. 8040875

Sample Code 211-58E

Test Animal: Male young adult albino rats (approximately 7 weeks of age) of the Sprague Dawley strain* were procured, maintained in group cages in air conditioned quarters, provided continuous access to commercial laboratory feed and water and held for a conditioning period of at least 7 days.

Method: Animals were chosen at random from the conditioned animals, dosed as specified and maintained individually in screen bottom cages with continuous access to feed and water for a two week observation period. Observations were made at hourly intervals for 5 hours after dosing and twice daily for the remainder of the two week period. At termination, surviving animals were sacrificed. Gross post mortem examinations were performed on all animals on test and gross tissue alterations noted.

Method of Administration: stomach tubed

Concentration of Test Material: as submitted

Results:

| Dosage Level [1] (gm/kg) | | erage ghts (gms) Terminal | Mortal: Number [2] | Lty Day [3] |
|--------------------------|-----|---------------------------------|-----------------------|----------------|
| 5.0 | 196 | 279 | 0/10 | |

Oral LD₅₀: in excess of 5 gm/kg of body weight

- [1] Of test material
- [2] Number dead/number dosed
- [3] Period during which deaths were observed

* ARS/Sprague Dāwley; Madison, Wisconsin

Other Observations: Necropsies were done on all of the animals. Two of

the animals had lungs that were dark red in color. None of the remaining eight animals showed any re-

markable tissue alterations.



PRIMARY SKIN IRRITATION

Client Ashland Chemical Company

WARF Institute No. 8040875

Sample Code 211-58E

Test Animal: Young adult rabbits (approximately 14 weeks of age) of the New Zealand white strain weighing 2.5 to 3.5 kg were procured, maintained individually in screen bottom cages in air conditioned quarters, provided continuous access to commercial laboratory feed and water and held for a conditioning period of at least 7 days.

Method: Conditioned animals were chosen at random, treated and maintained as specified for the conditioning period.

The hair was clipped from the back and flanks of the animal. The test material was applied to two areas on each rabbit, I abraded area, and I intact area, in the amount of 0.5 ml per area in the case of liquids or 0.5 gm per area in the case of solids. The treated areas were covered with a gauze patch and taped to maintain the test material in contact with the skin and decrease the rate of evaporation. The animals were immobilized for a 24 hour period at which time the coverings were removed and the degree of crythema and edema were recorded according to the scale below. A second reading was taken at 72 hours. The average of the 24 and 72 hour readings were used to determine the primary irritation index for the sample.

Concentration of Test Material: as submitted

Results:

| Animal | 24 Ho | | 72 Hours (1) | | | |
|---|---|--|---|--|--|--|
| Number | Abraded Er. Ed. | Unabraded Er. Ed. | Abraded Er. Ed. | Unabraded Er. Ed. | | |
| 265 269 278 280 282 270 Score | 1 0 1 0 1 1 1 1 1 0 1 0 24-hour | 1 0 1 0 1 1 1 1 1 0 1 0 | 0 0 1 0 0 0 0 0 0 0 0 0 72-hour | 0 0 1 0 0 0 0 0 0 0 0 0 | | |

Primary Skin Irritation Index (2): 0.8

(1) Score equals sum of erythems and edems readings.

(2) Skin irritation index equals average of 24 and 72 hour scores.

| Erythema and Eschar Formation Slight erythema Defined erythema | Score 1 | Edema Formation Slight edema (barely | Score |
|--|------------|---------------------------------------|-------|
| Moderate to severe erythems | 2 3 | perceptible) Defined edema (edges | 1 |
| Severe erythema to slight eschar formation | 4 | definite rising) Moderate edema (area | 2 |
| | | raised 1 mm) Severe edema (raised | 3 |
| | | more than 1 mm) | 4 |

WARF INSTITUTE, INC.

MADISON, WISCONSIN

EYE INRITATION

Client Ashland Chemical Company

WARF Institute No. 8040875

Sample Code 211-58E

Test Animal: Young adult rabbits (approximately 14 weeks of age) of the New Zealand white strain weighing 2.5 to 3.5 kg were procured, maintained individually in screen bottom cages in air conditioned quarters, provided continuous access to commercial laboratory feed and water and held for a conditioning period of at least 7 days.

Method: Conditioned animals were chosen at random, treated and maintained as specified for the conditioning period.

For each animal treated, one-tenth of a milliliter (0.1 gm for solids) of the test substance was instilled into one eye and the untreated eye served as a control. The reaction to the test material was read according to the scale of scoring for damage at specified times after instillation. Any residue of the test material and accumulated discharge were flushed from the eyes each time they were scored.

Concentration of Test Sample: as submitted

Special Washing: none

Results:

| | Rabbit | COTE | u | | | onjunctive | |
|------|--------|---------|-------|------------|----------|------------|--|
| | Munber | Opecity | Area | Iris | Redness | Chemosis | Discharge |
| | 13 | 0 . | 0 | 0 | 0 | 0 | |
| | 14 | 0 | 0 | Ŏ | ŏ | | 0 |
| 24 | 15 | 0 | . 0 | ŏ | ŏ | 0 | 0 . |
| Hour | 16 | 0 | Ò | ŏ | Ξ. | 0 | 0 |
| | 17 | Ō | Ö | | 0 | 0 | 0 |
| | 18 | ŏ | Ŏ | ŏ | 1 | 0 | 1 |
| | | • | U | U | 1 | 0 | .0 |
| | | | Eye | Irritation | Score: | L.0 | ************************************** |
| | 13 | ٥ | - 0 | 0 | • | _ | |
| | 14 | Õ | ŏ | ŏ | 0 | 0 | 0 |
| 48 | 15 | ŏ | | I | 0 | 0 | 0 |
| Hour | 16 | ŏ | 0 | 0 | 0 | 0 | 0 |
| | _17 _ | Ŏ | 0 | 0 | 0 | 0 | 0 |
| | 18 | - | | 0 | 0 | 0 | 0 |
| | 10 | 0 | 0 | 0 | 0 | . 0 | Ŏ |
| | | • | Eye I | Fritation | Score: 0 | | |
| | 13 | 0 | | ٥ | | _ | |
| | 14 | Ŏ | ŏ | <u> </u> | 0 | 0 | 0 |
| 72 | 15 | ŏ | | 0 | 0 | 0 | 0 |
| Hour | 16 | ŏ | - | 0 | 0 | 0 | 0 |
| | 17 | ŏ | 0 | 0 | 0 | 0 | 0 |
| | 18 | ŏ | . 0 | 0 | 0 | 0 | 0 |
| | | U | 0 | 0 | 0 | 0 | 0 |

Eye Irritation Score: 0

Reports are submitted to clients on a confidential basis. No reference to the work, the results or to the Institute in any of advertising, news release or other public announcement may be made without written authorization from the Inst

REPORT

Analysis for

Primary Skin Irritation, Primary Eye Irritation, Acute Oral Toxicity

Description of Sample

Date Received

3-31-78

Reference Number

211-58F

Submitted by

Ashland Chemical Company

Janesville, WI

Richard M. Egan

5% 015 PERSION 01

Claimed Content

Results

Acute Oral LD₅₀: in excess of 5.0 grams per kilogram of body weight

Skin Irritation Index:

Eye Irritation Scores:

Method

Please see the attached protocols.

Remarks

In accordance with FHSA regulations, this product is not toxic orally, is not irritating to the skin, and is not irritating to the eyes.

by and for the WARF INSTITUTE, INC.

Date

May 11, 1978.

WARF Institute No.

8040876

ACUTE ORAL TOXICITY

Client Ashland Chemical Company

4" · 1

WARF Institute No. 8040876

Sample Code 211-58F

Test Animal: Male young adult albino rats (approximately 7 weeks of age) of the Sprague Dawley strain* were procured, maintained in group cages in air conditioned quarters, provided continuous access to commercial laboratory feed and water and held for a conditioning period

Method: Animals were chosen at random from the conditioned animals, dosed as specified and maintained individually in screen bottom cages with continuous access to feed and water for a two week observation period. Observations were made at hourly intervals for 5 hours after dosing and twice daily for the remainder of the two week period. At termination, surviving animals were sacrificed. Gross post mortem examinations were performed on all animals on test and gross tissue

Method of Administration: stomach tubed

Concentration of Test Material: as submitted

Results:

| Dosage Level [1] (gm/kg) | Body Weig Initial | erage ghts (gms) Terminal | Mortality Number [2] Day [3] | į |
|--------------------------|----------------------|---------------------------------|------------------------------|---|
| 5.0 | 196 | 289 | 0/10 | - |

Oral LD50: in excess of 5 gm/kg of body weight

[1] Of test material

[2] Number dead/number dosed

[3] Period during which deaths were observed

* ARS/Sprague Dawley; Madison, Wisconsin

Other Observations: Necropsies were done on all of the animals. Two of the animals had hemorrhagic content in the small intestine. None of the remaining eight animals showed any remarkable tissue alterations.



PRIMARY SKIN IRRITATION

Client Ashland Chemical Company

WARF Institute No. 8040876

Sample Code 211-58F

Test Animal: Young adult rabbits (approximately 14 weeks of age) of the New Zealand white strain weighing 2.5 to 3.5 kg were procured, maintained individually in screen bottom cages in air conditioned quarters, provided continuous access to commercial laboratory feed and water and held for a conditioning period of at least 7 days.

Method: Conditioned animals were chosen at random, treated and maintained as specified for the conditioning period.

The hair was clipped from the back and flanks of the animal. The test material was applied to two areas on each rabbit, I abraded area, and I intact area, in the amount of 0.5 ml per area in the case of liquids or 0.5 gm per area in the case of solids. The treated areas were covered with a gauze patch and taped to maintain the test material in contact with the skin and decrease the rate of evaporation. The animals were immobilized for a 24 hour period at which time the coverings were removed and the degree of erythema and edema were recorded according to the scale below. A second reading was taken at 72 hours. The average of the 24 and 72 hour readings were used to determine the primary irritation index for the sample.

Concentration of Test Material: as submitted

Results:

| | | 24 Ho | | | 72 Hours (1) | | | 1) | |
|------------------|-------------|-------|--------------|-----|--------------|------|-----|--------------|---|
| Animal Number | Abra Er. | Ed. | Unabi Er. | Ed. | | Ed. | | raded Ed. | |
| 265 | 1 | 0 | 7 | ^ | | _ | _ | | |
| 269 | • | | _ | 0 | 1 | 0 | 1 | 0 | |
| - | T | 0 | 1 | 0 | 2 | 0 | 2 | 0 | |
| 278 | 1 | 1 | 1 | 0 | 1 | • | - | - | |
| 280 | • | ~ | • | - | _ | 0 | 0 | 0 ~ | |
| | 1 | 0 | Ţ | 0 | 0 | 0 | 0 | 0 | ÷ |
| 282 | 1 | 0 | 1 | 0 | 1 | Ō | Ť | | |
| 270 | 1 | 0 | | • | _ | | Ţ | 0 | |
| - | <u>.</u> | _ | Ţ | 0 | 1 | 0 | 1 | 0 | |
| Score | 24- | hour | 1.1 | • | 72- | hour | 0.9 | • | |

Primary Skin Irritation Index (2): 1.0

(1) Score equals sum of erythema and edema readings.

(2) Skin irritation index equals average of 24 and 72 hour scores.

| Erythema and Eschar Formation Slight erythema | Score | Edema Formation | Score |
|--|-------|--------------------------------------|-------|
| Defined erythema | 2 | Slight edema (barely | _ |
| Moderate to severe erythema | 3 | perceptible) Defined edema (edges | 1 |
| Severe erythema to slight eschar formation | | definite rising) | 2 |
| Cocuat Tormation | 4 | Moderate edema (area | |
| | | raised 1 mm) | 3 |
| | | Severe edema (raised | |
| | | more than 1 mm) | 4 |

WARF INSITIUTE, INC.

MADISON, WISCONSIN

EYE IRRITATION

Client Ashland Chemical Company

WARF Institute No. 8040876

Sample Code 211-58F

Test Animal: Young adult rabbits (approximately 14 weeks of age) of the New Zealand white strain weighing 2.5 to 3.5 kg were procured, maintained individually in screen bottom cages in air conditioned quarters, provided continuous access to commercial laboratory feed and water and held for a conditioning period of at least 7 days.

Method: Conditioned animals were chosen at random, treated and maintained as specified for the conditioning period.

For each animal treated, one-tenth of a milliliter (0.1 gm for solids) of the test substance was instilled into one eye and the untreated eye served as a control. The reaction to the test material was read according to the scale of scoring for damage at specified times after instillation. Any residue of the test material and accumulated discharge were flushed from the eyes each time they were scored.

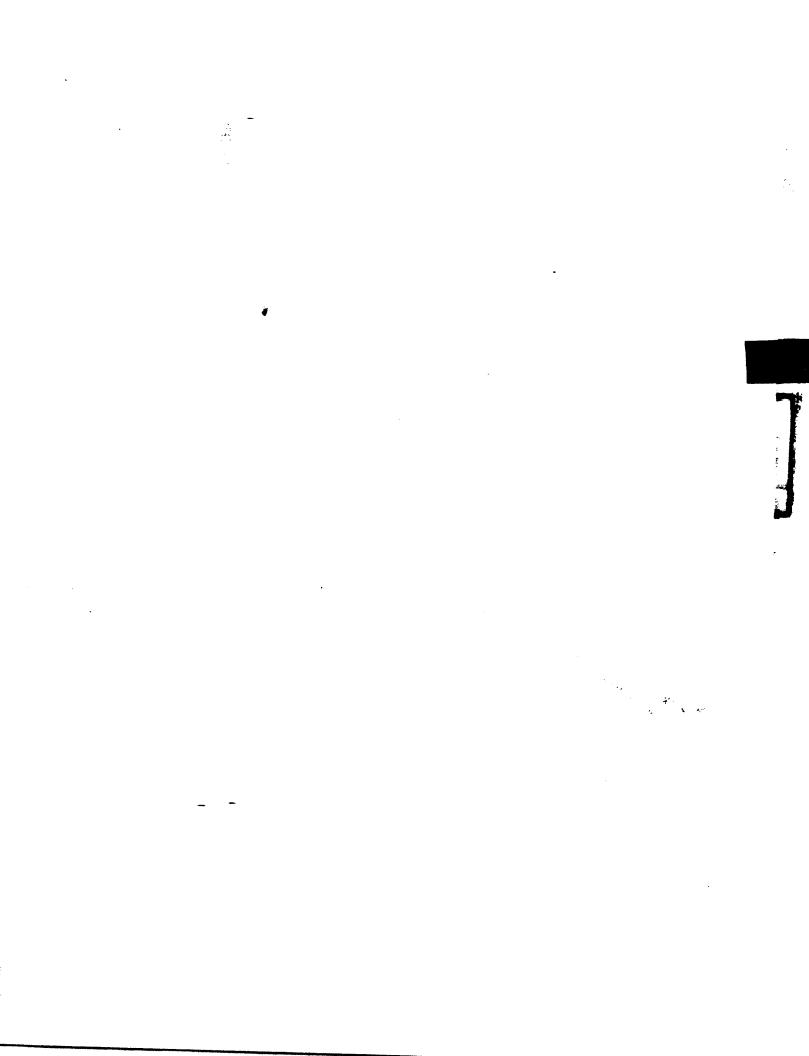
Concentration of Test Sample: as submitted

Special Washing: none

Results:

| | Rabbit | Corne | 84 | | | Conjunctiva | • |
|------------|-------------------------------------|-----------------------|------------------|-----------------------|-----------------------|------------------|-----------------------|
| | Number | Opacity | Area | Iris | Redness | Chemosis | Discharge |
| 24 Hour | 19 20 21 22 | 0 0 0 | 0 0 0 | 0 | 0 0 0 | 0 0 | 0 0 0 |
| | 23 24 | 0 | 0 | 0 0 0 | 0 0 0 | 0 0 0 | 0 0 0 |
| | | | Eye | Irritation | Score: | 0 | ÷' |
| 48 Hour | 19 20 21 22 23 _ 24_ | 0 0 0 0 0 | 0 0 0 0 | 0 0 0 0 0 | 0 0 0 0 | 0 0 0 0 | 0 0 0 0 0 |
| | | | Eye | Irritation | Score: | 0 | • |
| 72 Hour | 19 20 21 22 23 24 | 0 0 0 0 0 | 0 0 0 0 | 0 0 0 0 0 | 0 0 0 0 0 | 0 0 0 0 | 0 0 0 0 0 |

Eye Irritation Score: 0



Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

Attachment 10:

•

Toxicity Studies for Ashland Oil Company [PEQ 68410-69-5, 4% and 8% dispersions]

Carisoff 222 AT =10 (4%, 8% solds (H20) Cecular Stritation Clark 450

TOXICITY STUDIES

FOR

ASHLAND CHEMICAL COMPANY

COMPILED BY:
Lois Green

REPORTED:

August 7, 1973

REQUESTED BY:

Dr. N.S. Salomons

EYE IRRITATION STUDY

Federal Hazardous Substances Labeling Act

Varisoft 222 4% Solution
Varisoft 222 8% Solution

DRAIZE RABBIT EYE IRRITATION STUDY PROCEDURE FEDERAL HAZARDOUS SUBSTANCES LABELING ACT

A group of 12 albino rabbits was used in this study to determine the toxicity of the substance $_{\rm S}$ submitted to eye mucosa. A series of 6 rabbits was used for testing **each** substance.

One tenth of a milliliter of the product under test was instilled into the conjunctival sacs of the test animals. All treated eyes were unwashed. Ocular evaluations were made with the unaided eye. These evaluations were made at 24, 48 and 72 hours.

The cornea is scored on the basis of the density of the opacity and the total area involved. The iris is scored on the intensity or degree of inflammation exhibited; and the palpebral and bulbar mucosae are scored on the extent of chemosis, hyperemia and discharge.

DRAIZE SCALE FOR SCORING OCULAR LESIONS

| l. | Corn | ea |
|----|------|--|
| | Α. | Opacity-Degree of Density (area which is most dense taken for reading) |
| | | Scattered or diffuse area-details of iris clearly visible |
| | | slightly obscured |
| | | Opalescent areas, no details of iris visible, size of |
| | | pupil barely discernible |
| | В. | Opaque, iris invisible4 Area of Corneal damage involved |
| | - • | One quarter of area (or less) but not zero |
| | | Greater than one quarter, less than one-half |
| | | Greater than one half, less than three quarters |
| | | Greater than three quarters up to whole area |
| 2. | Iris | |
| | A. | Values |
| | | Folds above normal, congestion, swelling circumcorneal injection (any one or all of these or combination of any thereof), iris |
| | | still reacting to light, (sluggish reaction is positive) |
| | | one or all of these) |
| 3. | Conj | ınctivae |
| | Α. | Redness (refers to palpebral and bulbar conjunctivae excluding cornea and iris) |
| | | Vessels definitely injected above normal |
| | | easily discernible 2 |
| | В. | Diffuse beefy red 3 Chemosis |
| | | Any swelling above normal (includes nictitating membrane) 1 |
| | | Obvious swelling with partial eversion of the lids |
| | | Swelling with lids about half closed |
| | C. | Swelling with lids about half closed to completely closed 4 Discharge |
| | | Any amount different from normal (does not include small amount |
| | | observed in inner canthus of normal animals) |
| | | to the lids |
| | | Score (A + B + C) x 2 Total maximum - 20 |
| | | The maximum total score is the sum of all scores obtained for the cornea, iris and conjunctivae. Total maximum score possible - 110 points |

SCORE SHEET

Product Tested

Varisoft 222

4% Solids

Animal No.

1 Unwashed

| | | • | | | | | |
|--------------------------------------|---|---|-----|------|------|------|-----|
| Day | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| Hour | 1 | | Dai | ly T | here | efte | |
| I— CORNEA | | | | | | | |
| A— Opacity | | | | | | | |
| B— Area Involved | | | | | | | |
| II— IRIS | | | | | | | |
| A— Evaluation | | | | | | | |
| III— CONJUNCTIVAE | | | | | | | ٠., |
| A- Hyperemia | 1 | | | | | | |
| B- Chemosis | | | | | | | |
| C— Discharge | | | | | | | |
| Total Points (Total Possible 110) | 2 | | | | | | ヿ |

Product Tested

Varisoft 222

ď

4% Solids

Animal No.

2 Unwashed

| Day | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|--------------------------------------|---|---|-----|------|------|------|---|
| Hour | 1 | | Dai | ly T | here | afte | |
| I— CORNEA | | | | | | | |
| A— Opacity | | | | | | | |
| B- Area Involved | | | | | | | |
| II— IRIS | | | | | | | |
| A— Evaluation | | | | | | | |
| III— CONJUNCTIVAE | | | | | | | - |
| A— Hyperemia | 1 | | | | | | |
| B Chemosis | | | | | | | |
| C- Discharge | | | | | | | |
| Total Points (Total Possible 110) | 2 | | | | | | |

Product, Tested

Varisoft 222

4% Solids

Animal No.

3 Unwashed

| | | 1 4 | | | | | |
|-----------------------------------|---|-----|-----|------|------|-------------|-----------|
| Day | | 1 | 3 | 4 | 3 | 6 | 7 |
| Hour | 1 | | Dai | iy T | bere | efte | r |
| I— CORNEA | | | | | | | |
| A Opacity | | | | | | | |
| B- Area Involved | | | | | | | |
| II— IRIS | | | | | | | —— |
| A Evaluation | | | | | | | |
| III— CONJUNCTIVAE | | | | | | | |
| A— Hyperemia | 1 | | | | | | |
| B- Chemosis | | | | | | | |
| C— Discharge | | | | | | | |
| Total Points (Total Possible 210) | 2 | | | | | | |

Product Tested

Varisoft 222

4% Solids

Animal No.

4 Unwashed

| Day | 1 | 2 | 3 | 4 | 5 | 6 | 7 |] |
|-------------------------------------|---|---|-----|------|------|-----------|-----------|--|
| Hour | 1 | | Dai | ly I | bere | afte | ┴ <u></u> | |
| I— CORNEA | | | | | | | | |
| A— Opacity | | | | | | | | |
| B- Area Involved | | | | | | | | |
| II— IRIS | | | | | | | | |
| A— Evaluation | | | | | | _ | | |
| III— CONJUNCTIVAE | | 1 | | | | ! | | |
| A Hyperemia | 1 | | | | | | 7 | a de la companya de l |
| B— Chemosis | | | | | | \exists | | |
| C— Discharge | | | 1 | | | | | |
| Total Points Total Possible (10) | 2 | | 7 | | | | 7 | |

Product Tested

Varisoft 222

4% Solids

Animai No.

5 Unwashed

| Day | 1 | 2 | | 3 | 4 | 5 | 6 | 7 |
|-------------------|---|---|---|-----|------|------|------|----|
| Hour | 1 | | D |)ai | ly T | bere | afte | r |
| I— CORNEA | | | | | | | | |
| A— Opacity | | | | | | | | |
| B— Area Involved | | | | | | | | |
| II— IRIS | | | | | | | | |
| A— Evaluation | | | | | | | | |
| III— CONJUNCTIVAE | | | | | | | | ŧ. |
| A— Hyperemia | 1 | | | | | | | |
| B Chemosis | | | | | | | | |
| C— Discharge | | | | | | | | |
| Total Points | 2 | | | | | | | |

Product Tested

Varisoft 222

4% Solids

Animal No.

6 Unwashed

| Day | Ť | 2 | 3 | 4 | 5 | 6 | 7 |
|-----------------------------------|---|---|-----|------|------|------|---|
| Hour | | | Dai | ly T | bere | afte | · |
| I— CORNEA | | | | | | | |
| A— Opacity | | | | | | | |
| B- Area Involved | | | | | | | |
| II— IRIS | | | | | | | |
| A— Evaluation | | | | | | | |
| III— CONJUNCTIVAE | | | | | | | |
| A— Hyperemia | 1 | | | | | | |
| B Chemosis | | | | | | | |
| C Discharge | | | | | | | |
| Total Points (Total Possible 110) | 2 | | | | | | |

Product Tested

Varisoit 222

8% Solids

Animal No.

1 Unwashed

| | <u> </u> | 1 | I | | | | |
|----------------------------------|----------|---|--------------|------|------|---|--------------|
| Day | 1 | 2 | 3 4 | 5 | 6 | 7 | |
| Hour | 1 | I | Daily ' | Ther | mfte | 7 | |
| I— CORNEA | | | | | | | |
| A— Opacity | | | | | | | |
| B— Area Involved | | | | | | | |
| II— IRIS | | | | | | | - |
| A— Evaluation | | | | | | | |
| III— CONJUNCTIVAE | | | | | | | |
| A— Hyperemia | 2 | 1 | | | | | , " . |
| B Chemosis | | | | | | | |
| C— Discharge | | | | | | | |
| Total Points Total Possible 1101 | 4 | 2 | | | | | |

Product Tested

Varisoft 222

8% Solids

Animai No.

2 Unwashed

| Day | | | 2 | 3 | 4 | 5 | 6 | 7 |
|--------------------------------------|---|----------|----------|-----|------|------|------|-----|
| Hour | | | | Dai | ly T | bere | afte | |
| I— CORNEA | | | | | | | | |
| A— Opacity | | | | | | | | |
| B- Area Involved | | | | | | | | |
| II— IRIS | | | | | | | | |
| A— Evaluation | | | | | | | | |
| III— CONJUNCTIVAE | | | | | | | | ٠., |
| A— Hyperemia | 2 | ? | 1 | | | | | |
| B— Chemosis | | | <u> </u> | | | | | |
| C— Discharge | | | | | | | | |
| Total Points (Total Possible 110) | 4 | <u> </u> | 2 | | | | | |

4 × 40

DRAIZE RABBIT EYE IRRITATION STUDY

Product Tested

Varisoft 222

8% Solids

Animal No.

3 Unwashed

| Day | | | 2 | 3 | 4 | 5 | 6 | 7 |
|-----------------------------------|---|---|---|-----|------|------|------|---|
| Hour | | | | Dai | ly T | here | afte | |
| I— CORNEA | _ | | | | | | | |
| A— Opacity | | | | | | | | |
| B- Area Involved | | | | | | | | |
| II— IRIS | | | | _ | | | | |
| A— Evaluation | | | | | | | | |
| III— CONJUNCTIVAE | | | | | | | | |
| A— Hyperemia | 2 | ? | 1 | | | | | |
| B Chemosis | | | | | | | | |
| C— Discharge | | | | | | | | |
| Total Points (Total Possible 110) | 4 | l | 2 | | | | | |

Product Tested

Varisoft 222

8% Solids

Animal No.

4 Unwashed

| Day | 1 | 2 | 3 | 4 | 5 | 6 | 7 | |
|----------------------------------|---|---|-----|-------|-----|-------|---|-----|
| lour | | | Dai | ily T | her | eefte | • | |
| - CORNEA | | | | | | | | |
| — Opacity | | | | | | | | |
| - Area Involved | | | | | | | | |
| i— iris | | | | | | | | |
| A— Evaluation | | | | | | | | |
| II— CONJUNCTIVAE | | | | | | | | |
| A— Hyperemia | 1 | | | | | | | 6°. |
| B— Chemoris | | | | | | _ | | |
| C- Discharge | | | | | | | | |
| Total Points Total Possible 110) | 2 | | | | | | | |

Product Tested

Varisoft 222

8% Solids

Animal No.

5 Unwashed

| Day | T | 2 | 3 | 4 | 5 | 6 | 7 |
|--------------------------------------|---|---|-----|------|------|-------|---|
| Hour | 1 | | Dai | ly T | here | after | |
| I— CORNEA | | | | | | | |
| A— Opacity | | | | | | | |
| B— Area Involved | | | | | | | |
| II— IRIS | | | | | | | |
| A— Evaluation | | | | | | | |
| III— CONJUNCTIVAE | | | | | | | |
| A- Hyperemia | 2 | 1 | | | | | |
| B— Chemosis | | | | | | | |
| C— Discharge | | | | | | | |
| Total Points (Total Possible 110) | 4 | 2 | | | | | |

Product Tested

Varisoft 222

8% Solids

Animal No.

6 Unwashed

| Day | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|-----------------------------------|---|---|-----|-----|----------|-------|---|
| Hour | 1 | | Dai | y T | here | after | |
| I— CORNEA | | | | | | | |
| A— Opacity | | | | | | | |
| B- Area Involved | | | | | | | |
| II— IRIS | _ | | | | | | |
| A— Evaluation | | | | | | | |
| III— CONJUNCTIVAE | | | | | - | | |
| A— Hyperemia | 2 | 1 | | | | | |
| B— Chemosis | | _ | | | | | |
| C- Discharge | | | | | | | _ |
| Total Points (Total Possible 110) | 4 | 2 | | | | | |

SUMMARY OF POINTS SCORED

Varisoft 222 4% Solids 8% Solids

SUMMARY OF POINTS SCORED

| | _ | Total Points | 12 | 32 | | | | | |
|---------------|---|--------------|-------|-------|--|---|----------|----|----|
| | nds | 3 | | | | • | | | |
| EYES | # seconds | 2. | | | | | | | |
| EY | L 4 | 1 | | | | | | | |
| WASHED | M A | 3 | | | | | | | |
| WAS | $\frac{A}{2}$ $\frac{N}{s}$ $\frac{I}{s}$ $\frac{M}{s}$ | 2 | | | | | | | |
| | Al S | 1 | | | | | | | |
| _ | | | | | | | <u> </u> | | |
| _ | | | | | | | | | |
| = | | 9 | 2 | 9 | | | | | |
| = | #1 | - | | | | | | | |
| (ES | #1 | 5 6 | 2 2 | 9 9 | | | | | |
| EYES | ᆈ | - | | | | | | ÷* | w. |
| ı | M A L | 5 | 2 | 9 | | | | + | 47 |
| ŀ | T W | 4 5 | 2 2 | 2 6 | | | | | |
| UNWASHED EYES | I M A L | 3 4 5 | 2 2 2 | 6 2 6 | | | | ** | |

Bio-Toxicology Laboratorica . Toxicity and Applied Research Studies - Animal and Human

PRIMARY IRRITATION STUDY

Federal Hazardous Substances Labeling Act

Varisoft 222 4% Solids 8% Solids

METHOD FOR PRIMARY IRRITATION-RABBIT SKIN FEDERAL HAZARDOUS SUBSTANCES LABELING ACT

The intact and abraded skin of albino rabbits was used for this study. A series of 6 rabbits was used for testing substance. The hair was clipped from the backs with the aid of angora chippers. Two areas of the back, placed approximately ten centimeters apart, were designated for the positions of the patches. One area was abraded by making four epidermal incisions (two perpendicular to two others in the area of the patch.) The patches consisted of two layers of light gauze cut in squares (2.5 cm. on the side). The patches were secured to the area by thin bands of adhesive tape. The material to be tested 48.5 ml.) was introduced beneath the patch. The entire trunks of the animals were then wrapped in clear plastic trunk bands. The trunk bands help to hold the patches in position and retards evaporation of volatile substances during the twenty-four hour exposure. The compound under test was applied so that there were two applications (one intact and one abraded) to each of six animals. The animals were immobilized in a special holder during the twenty-four exposure period. Upon removal of the patches the resulting reactions were evaluated on the basis weighted scores. Evaluations were again made after seventy-two hours. The final score represents an average of the twenty-four and seventy-two hour readings.

METHOD OF POINT SCORING

FOR

EVALUATION OF SKIN REACTIONS

| Α. | Erythema and Eschar Formation Very slight erythema (barely perceptible). Well defined erythema Moderate to severe erythema Severe erythema (beet redness) to slight eschar formation (injuries in depth) | 3 |
|----|---|-------------|
| - | (injuries in depth) | 4 |
| | Total possible erythema score | 4 |
| В. | Edema Formation Very slight edema (barely perceptible) Slight edema (edges of area well defined by definite raising) Moderate edema (area raised approximately 1 mm.) Severe edema (raised more than 1 mm. and extending beyond area of exposure) | 1 2 3 |
| | Total possible edema score | 4 |
| • | Total possible score for primary irritation | 8 8 |

Primary Irritation Index

2 or less.....mild irritant
2 - 5.....moderate irritant
5 or above.....severe irritant
6 or above.....severe sensitizer

SCORE SHEETS

PRIMARY IRRITATION STUDY

Product Tested

Varisoft 222

4% Solids

Test Method

Draine Woodard and Calvery

| A B. | | | RABE | oit skin | | |
|----------|-------|---------|---------|----------|---------|---|
| | IIMAL | INT | ACT | ABR | ADED | COMBINED |
| NO. | SEX | 24 HRS. | 72 HRS. | 24 HRS. | 72 HRS. | AVERAGE |
| 1 | M | 0 | 0 | 0 | 0 | |
| 2 | F | 0 | 0 | 0 | 0 | |
| 3 | F | 0 | 0 | 0 | 0 | |
| 3 | M | 0 | 0 | 0 | 0 | 0.0 |
| 5 | M | 0 | . 0 | 0 | 0 | , |
| į | F | 0 | 0 | 0 | 0 | - |
| | | | | | | |
| | | | | | • | * |
| | | | | | | |
| | | | | | | |
| AV | ERAGE | 0. | 0 | 0. | 0 | |

Primary Irritation Index of Compound 0.0

PRIMARY IRRITATION STUDY

Product Tested

Varisoft 222 o% Solids

Test Method

Draine Woodurd and Calvery

| X %T: | 73 × 3 × | | RABB | IT SKIN | | |
|-------|------------|---------|----------|---------|---------|------------------|
| | IMAL | INT | ACT | ABR | ADED | COMBLVED |
| NO | ZEX | 24 HRS. | 72. HRS. | 24 HRS. | 72 HRS. | AVERAGE |
| • | M | 0 | 0 | 0 | 0 | |
| 2 | F | 0 | 0 | 0 | 0 | |
| 3 | F | 0 | 0 | 0 | 0 | |
| | M | 0 | 0 | 0 | 0 | 0.0 |
| 5 | . M | 0 | · 0 | 0 | 0 | |
| • | F | 0 | 0 | o | 0 | - |
| | | | | | | |
| | | | | | | * * * • • |
| | | | | | | |
| AVE | RĀGE | - 0.0 | | 0.1 | | |

Primary Irritation Index of Compound 0.0

ACUTE ORAL TOXICITY STUDY

Varisoft 222 4% Solids 8% Solids

METHOD - ACUTE ORAL TOXICITY

A group of approximately 30 albino male and female rats, fasted for twenty-four hours were employed to establish an LD₅₀ range for each product under test.

Young adult rats which had not been used for previous test purposes were assigned to various dose levels at random. Both sexes were equally distributed.

The product under test was placed in a glass syringe and introduced through the esophagus into the stomach with a stainless steel catheter.

Animals on the same dosage level were then placed in a common cage with free access to food and water. The animals were observed daily for a two week period. No postmortem, or histopathology examinations were performed in this particular study.

SCORE SHEETS

ACUTE ORAL TOXICITY ASSAY

Varisoft 222

EXPERIMENTAL DATA

Dotages 0.5 cc./Kg. - 16.0 cc./Kg.

Animals Fasted male & female albino rats

Concentration 4% Solids in aqueous solution

Weights 200-300 grams

| | T | | | | | | | | | | | | | | | | | |
|-------|---------|---------------|---|---|---|--------------|----------|------|-----|-----|------|-------|----|----|--|----|---------------|----------|
| Group | No. | Dose | | _ | , | , | Nu | mber | end | Day | of D | eachs | • | | | | τ | ocal |
| No. | Animale | Lovel | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | s • | D. |
| t | 5 | 0.5 ce/Ke | | | | | | | | | | | | | | | 5 | 0 |
| ti | 5 | 1.0 e.e.Ke. | | | | | | | | | | | | | | | | 1 |
| 111 | | 2.0 ecike | | | | | | | | | | | | | | | <u> </u> | 0 |
| IV | 5 | 4 .0 e.c./Ke. | | | | | | | | | | | | | - | | <u>5</u> 5 | <u> </u> |
| v | | 8.0 c.c./Ke. | | | | | | | | | | _ | | | | | | 0_ |
| VI | | 16. Galke | | | | \vdash | | | | | | | | | | | 5 | - |
| VII | | c.c./Kg. | | | | | | | | | | | | | | | 5 | 0_ |
| VIII | | e.e./Kg. | | | | | | | | | | | | | | - | | |
| 1X | | c.e./Ke. | | | | | \vdash | | | | | | | | | - | | |
| x | | e.e./Ks. | | | | | _ | | | | | | | | | ╌╢ | | |

OBSERVATIONS.

Animals did not exhibit any effects from the test material.

Eating habits and behavior patterns remained normal throughout the observation period.

Equally non-toxic to males & females.

LD. - Over 16.0 cc./Kg.

LD_{ee} = Over 16.0 cc./Kg. (95% Confidence Limits = Not Established)

 $LD_{les} = Over 16.0 cc./Kg.$

D = Deaths

" 8 - Survivale

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ACUTE ORAL TOXICITY ASSAY Varisoft 222

EXPERIMENTAL DATA

Dosages

0.5 cc./Kg. - 16.0 cc./Kg.

Animak

Fasted male & female albino rats

8% Solids in aqueous dispersion Weights

200-300 grams

| Group | No. | Doos | | | | | Nu | mber | and | Dev | of D | eaths | • | | | | Te | red . |
|-------|---------|--------------|---|---|---|---|----|------|-----|-----|------|-------|----|----|----|----|-----|-------|
| No. | Animale | Lovel | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 8 * | p* |
| 1 | 5 | 0.5 duka | { | | | | | | | | | | | | | | 5 | 0 |
| 11 | 5 | 1.0 e.c.iKe. | | | | | | | | | | | | | | | 5 | 0 |
| 111 | 5 | 2.0 ec.iKs. | | | | | | | | | | | | | | | 5 | 0 |
| IV | 5 | 4.0 cc/Ke | | | | | | | | | | | | | | | 5 | 0 |
| v | 5 | 8.0eclKe | | | | | | | | _ | | | | | | | 5 | 0 |
| VI | 5 | 16. Onelike. | | | | | | | | | | | | | | | 5 | 0 |
| VII | | c.c.lKe. | | | | | | | | | | | | | | | | |
| VIII | | c.c.iKe. | | | | | | | | | | | | | | | | |
| 1X | | . celka | | | | | | | | | | | | | | | | |
| x | | e.c.iKg. | | | | | | | | | | | | | | | | |

OBSERVATIONS.

Animals did not exhibit any effects from the test material.

Eating habits and behavior patterns remained normal throughout the observation period.

Equally non-toxic to males and females.

Over 16.0 cc./Kg.

Over 16.0 cc./Kg. (95% Confidence Limits = Not Established)

Over 16.0 cc./Kg.

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SUMMARY & CONCLUSIONS

SUMMARY & CONCLUSIONS
OF TOXICITY DATE
SAMPLE Varisoft 222 4% Solids

(See Individual Score Sheets for Detailed Information)

STUDIES PERFORMED

- X DRAIZE EYE IRRITATION
- X PRIMARY IRRITATION
- X ACUTE ORAL TOXICITY
 ACUTE DERMAL TOXICITY
 DAY SUBACUTE TOXICITY
 ACUTE INHALATION

| DRAIZE EYE | IRRITATIO | N STUDY | ⁶ albino rabbits | | | | | | |
|--------------|-----------------|---------------|-----------------------------|---------------|-----------------|---------------|--|--|--|
| | 6 eyes u | nwashed | eyes wa | shed | eyes w | ashed | | | |
| STRUCTURE | Total Points | Mean Value | Total Points | Mean Value | Total Points | Mean Value | | | |
| Cornea | 0 | 0.0 | · | | | | | | |
| Iris | 0 | 0.0 | | | | | | | |
| Conjunctivae | 12 | 2.0 | | , | | | | | |

6

Requires labeling under the Federal Hazardous Substances Act.

X Does not require labeling under the Federal Hazardous Substances Act.

PRIMARY IRRITATION STUDY

albino rabbits

Primary Irritation Index:

X Non-primary irritant (score 0.0)
Mild primary irritant (score 0.1-2.0)

Moderate primary irritant(score 2.1-5.0) Severe primary irritant (score over 6.0)

Requires labeling under the Federal Hazardous Substances Act.

Does not require labeling under the Federal Hazardous Substances Act.

| ACUTE ORAL TOXICITY | X | Acute Oral LD ₅₀ Study - 30 albino rats | |
|------------------------------------|-----|--|--|
| (single parenteral dose) | | F.H.S.L.A. Procedure - 10 albino rats | |
| Acute Oral LD ₅₀ Study: | | Federal Hazardous Substances | |
| | | Act Procedure: | |
| LD ₅₀ - 95% Confidence | | Dosage: 5.0 c.c. or 5.0 gms./Kg. | |
| Over 16.0 cc./Kg. Limits | | Deaths: | |
| Not Established | | | |
| Requires labeling under the F | ede | ral Hazardous Substances Act. | |
| X Does not require labeling und | er | the Federal Hazardous Substances Act. | |

SUMMARY & CONCLUSIONS
OF TOXICITY DATE
SAMPLE_Varisoft 222 8%Solids

(See Individual Score Sheets for Detailed Information)

STUDIES PERFORMED

- X DRAIZE EYE IRRITATION
- X PRIMARY IRRITATION
- ACUTE ORAL TOXICITY
 ACUTE DERMAL TOXICITY
 DAY SUBACUTE TOXICITY
 ACUTE INHALATION

| DRAIZE EYE | IRRITATIO | N STUDY | ⁶ albino rabbits | | | | | | |
|--------------|-----------------|---------------|-----------------------------|---------------|-----------------|---------------|--|--|--|
| | 6 eyes u | nwashed | eyes wa | ashed | eyes w | ashed | | | |
| STRUCTURE | Total Points | Mean Value | Total Points | Mean Value | Total Points | Mean Value | | | |
| Cornea | 0 | 0.0 | | | ł | | | | |
| Iris | 0 | 0.0 | | | | | | | |
| Conjunctivae | 32 | 5.3 | | | | | | | |

Requires labeling under the Federal Hazardous Substances Act.

X Does not require labeling under the Federal Hazardous Substances Act.

PRIMARY IRRITATION STUDY

6 albino rabbits

Primary Irritation Index:

X Non-primary irritant (score 0.0)
Mild primary irritant (score 0.1-2.0)

Moderate primary irritant(score 2.1-5.0) Severe primary irritant (score over 6.0)

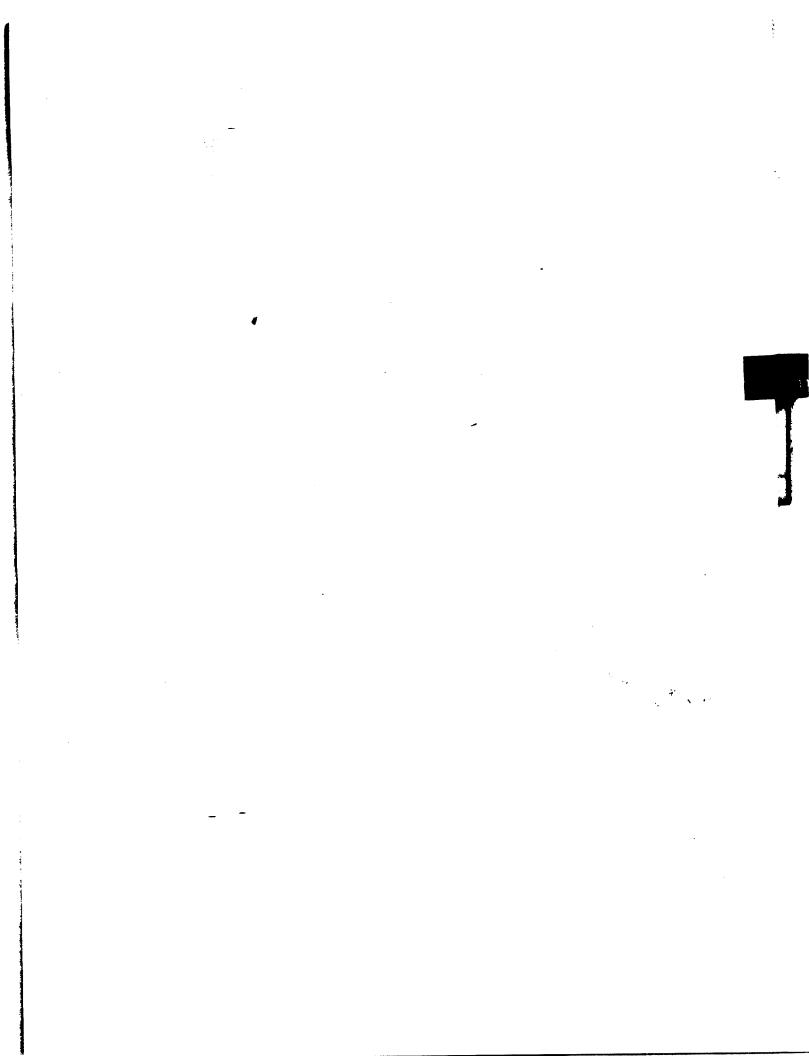
Requires labeling under the Federal Hazardous Substances Act.

XDoes not require labeling under the Federal Hazardous Substances Act.

| ACUTE ORAL TOXICITY (single parenteral dose) | X Acute Oral LD ₅₀ Study - 30 albino rats F.H.S.L.A. Procedure - 10 albino rats |
|--|---|
| Acute Oral LD ₅₀ Study: | Federal Hazardous Substances Act Procedure: |
| LD ₅₀ - 95% Confidence Over 16.0 cc./Kg. Limits | Dosage: 5.0 c.c. or 5.0 gms./Kg. Deaths: |
| Not Established | • |
| Requires labeling under the Fe | ederal Hazardous Substances Act |

Requires labeling under the Federal Hazardous Substances Act.

X Does not require labeling under the Federal Hazardous Substances Act.



Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

Attachment 11:

#

Report to Ashland Chemical Company - Acute Toxicity Studies with Varisoft 222 [PEQ 68410-69-5, 4% dispersion]

Industrial BIO-TEST Laboratories, Inc.

1810 FRONTAGE ROAD NORTHBROOK, ILLINOIS 60062

Obral 2000 Dermal > Frital Cleular > Frital 4%

REPORT TO

ASHLAND CHEMICAL COMPANY

ACUTE TOXICITY STUDIES WITH VARISOFT 222

MARCH 15, 1973

IBT NO. 601-02910

June

• • • . **-** -

Industrial BIO-TEST Laboratories, Inc.

1810 FRONTAGE ROAD NORTHBROOK, ILLINOIS 60062

March 15, 1973

Mr. Robert B. McConnell Ashland Chemical Company Division of Ashland Oil, Inc. Chemical Products Division 2001 Afton Road Janesville, Wisconsin 53545

Dear Mr. McConnell:

Re: IBT No. 601-02910 - Acute Toxicity

Studies with Varisoft 222

We are submitting herewith our laboratory report dated

March 15, 1973, prepared in connection with the above study.

very truly yours,

J. C. Calandra

President

JCC/kjl

REPORT TO

ASHLAND CHEMICAL COMPANY

ACUTE TOXICITY STUDIES WITH VARISOFT 222

MARCH 15, 1973

IBT NO. 601-02910

I. Introduction

A sample identified as VARISOFT 222 (4% Solids Dispersion),

Lot No. 152-12, was received from Ashland Chemical Company for
toxicological evaluation. The following studies were conducted:

Acute Oral Toxicity Study - Albino Rats

Eye Irritation Test - Albino Rabbits

Primary Skin Irritation Test - Albino Rabbits

II. Summary

The results of the acute toxicity studies with VARISOFT 222 (4% Solids Dispersion), Lot No. 152-12, are summarized below.

| Т | e | s | t |
|---|---|---|---|
|---|---|---|---|

Results

Acute Oral Toxicity Study Albino Rats

 $LD_{50} > 34,600 \text{ mg/kg}$

Eye Irritation Test -Albino Rabbits

Minimally Irritating (11.8/110.0)

Primary Skin Irritation Test Albino Rabbits

Mildly Irritating (1.9/8.0)

Respectfully submitted,

INDUSTRIAL BIO-TEST LABORATORIES, INC.

Report prepared by:

Larerten Vackleman

Beverley Kretchmar

Technician Acute Toxicity

Report approved by:

Carmen Mastri B S

Carmen Mastri, B. S. Senior Group Leader

Acute Toxicity

M. L. Keplinger, Ph. D.

Manager, Toxicology

chm

III. Investigational Procedures

A. Acute Oral Toxicity Study - Albino Rats

Young albino rats of the Charles River strain (COBS)* were used as test animals. All animals were kept under observation for five days prior to experimental use, during which period they were checked for general physical health and suitability as test animals. The animals were housed in stock cages and were permitted a standard laboratory diet plus water ad libitum, except during the 16-hour period immediately prior to oral intubation when food was withheld.

Initial screening was conducted in order to determine the general level of toxicity of the test material. Selected groups of four albino rats each (two males and two females) were administered the test material at several dose levels. All doses were administered directly into the stomachs of the rats using a hypodermic syringe equipped with a ball-tipped intubating needle.

After oral administration of the test material, the rats were housed individually in suspended, wire-mesh cages and observed for the following 14 days. Initial and final body weights and reactions were recorded.

A necropsy was conducted on all animals sacrificed at the end of the 14-day observation period.

^{*} Charles River Breeding Laboratories, Inc., North Wilmington, Mass.

At the end of the observation period, the acute oral median lethal dose (LD $_{50}$) of the test material was determined.

B. Eye Irritation Test - Albino Rabbits

Young albino rabbits of the New Zealand strain were used to evaluate the eye irritating properties of the test material. The test method was patterned after that of Draize et al.*

The test material was instilled into the conjunctival sac of the right eye of each rabbit according to the treatment procedure presented in Table I. The left eye of each animal served as a control. At each scoring interval the cornea, iris, and palpebral conjunctiva were examined and graded for irritation and injury according to a standard scoring system*. The maximum possible score at any one examination and scoring period is 110 points, which indicates maximal irritation and damage to all three ocular tissues. Zero score indicates no irritation. The scoring system is presented in Table II. In this scoring system, special emphasis is placed upon irritation or damage to the cornea, while less emphasis is placed upon damage to the iris and conjunctiva.

After completion of the test, the scores were analyzed, and a descriptive eye irritation rating was assigned to the test material.

The criteria used for assignment of the descriptive rating are the frequency, the extent, and the persistence of irritation or damage which occur to the three ocular tissues.

^{*} Draize, John H., Woodard, Geoffrey, and Calvery, Herbert O., "Methods for the Study of Irritation and Toxicity of Substances Applied Topically to the Skin and Mucous Membranes," J. Pharm. & Exp. Ther. 82, 377 (1944).

TABLE I

Eye Irritation Test - Albino Rabbits

Treatment Procedure

| Test Material | Animals Evaluated | Form Administered | Quantity of Test Material Administered | Contact Period (seconds) | Volume of Wesh | Scoring Intervale |
|---------------|--------------------|----------------------|--|--------------------------------|----------------|--|
| VARISOFT 222 | 9 | Undiluted | 0. 1 ml | Unlimited | | One minute, one, 24, and 72 hours, and 7 |

TABLE II

Eye Irritation Test - Albino Rabbits

Scale of Weighted Scores for Grading the Severity of Ocular Lesions

| Tissues Opacity (A) Opacity - Degree of density (area which is dense is taken for reading). Scattered or diffuse area, details of iris clearly visible. Easily discernible translucent areas, details of iris slightly obscured. Opalescent areas, no details of iris visible, size of pupil barely discernible Opaque, iris invisible Area of Cornea Involved (B) One quarter (or less) but not zero Greater than one-quarter but less than one-half. Greater than one-half but less than three-quarters. Greater than three-quarters, up to whole area. Score equals A x B x 5 Total maximum = 80 Iris Values (A) Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof), iris still reacting to light (sluggish reaction is | |
|--|----------|
| Opacity - Degree of density (area which is dense is taken for reading). Scattered or diffuse area, details of iris clearly visible. Easily discernible translucent areas, details of iris slightly obscured. Opalescent areas, no details of iris visible, size of pupil barely discernible Opaque, iris invisible Area of Cornea Involved (B) One quarter (or less) but not zero Greater than one-quarter but less than one-half. Greater than one-half but less than three-quarters. Greater than three-quarters, up to whole area. Score equals A x B x 5 Total maximum = 80 Iris Values (A) Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof), iris still | Grading |
| Opacity - Degree of density (area which is dense is taken for reading). Scattered or diffuse area, details of iris clearly visible. Easily discernible translucent areas, details of iris slightly obscured. Opalescent areas, no details of iris visible, size of pupil barely discernible Opaque, iris invisible Area of Cornea Involved (B) One quarter (or less) but not zero Greater than one-quarter but less than one-half. Greater than one-half but less than three-quarters. Greater than three-quarters, up to whole area. Score equals A x B x 5 Total maximum = 80 Iris Values (A) Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof), iris still | |
| dense is taken for reading). Scattered or diffuse area, details of iris clearly visible. Easily discernible translucent areas, details of iris slightly obscured. Opalescent areas, no details of iris visible, size of pupil barely discernible Opaque, iris invisible Area of Cornea Involved (B) One quarter (or less) but not zero Greater than one-quarter but less than one-half. Greater than one-half but less than three-quarters. Greater than three-quarters, up to whole area. Score equals A x B x 5 Total maximum = 80 Iris Values (A) Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof), iris still | |
| Scattered or diffuse area, details of iris clearly visible. Easily discernible translucent areas, details of iris slightly obscured. Opalescent areas, no details of iris visible, size of pupil barely discernible Opaque, iris invisible Area of Cornea Involved (B) One quarter (or less) but not zero Greater than one-quarter but less than one-half. Greater than one-half but less than three-quarters. Greater than three-quarters, up to whole area. Score equals A x B x 5 Total maximum = 80 Iris Values (A) Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof), iris still | |
| clearly visible. Easily discernible translucent areas, details of iris slightly obscured. Opalescent areas, no details of iris visible, size of pupil barely discernible Opaque, iris invisible Area of Cornea Involved (B) One quarter (or less) but not zero Greater than one-quarter but less than one-half. Greater than one-half but less than three-quarters. Greater than three-quarters, up to whole area. Score equals A x B x 5 Total maximum = 80 Iris Values (A) Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof), iris still | |
| of iris slightly obscured. Opalescent areas, no details of iris visible, size of pupil barely discernible Opaque, iris invisible Area of Cornea Involved (B) One quarter (or less) but not zero Greater than one-quarter but less than one-half. Greater than one-half but less than three-quarters. Greater than three-quarters, up to whole area. Score equals A x B x 5 Total maximum = 80 Iris Values (A) Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof), iris still | 1 |
| of iris slightly obscured. Opalescent areas, no details of iris visible, size of pupil barely discernible Opaque, iris invisible Area of Cornea Involved (B) One quarter (or less) but not zero Greater than one-quarter but less than one-half. Greater than one-half but less than three-quarters. Greater than three-quarters, up to whole area. Score equals A x B x 5 Total maximum = 80 Iris Values (A) Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof), iris still | |
| Opalescent areas, no details of iris visible, size of pupil barely discernible Opaque, iris invisible Area of Cornea Involved (B) One quarter (or less) but not zero Greater than one-quarter but less than one-half. Greater than one-half but less than three-quarters. Greater than three-quarters, up to whole area. Score equals A x B x 5 Total maximum = 80 Iris Values (A) Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof), iris still | 2 |
| size of pupil barely discernible Opaque, iris invisible Area of Cornea Involved (B) One quarter (or less) but not zero Greater than one-quarter but less than one-half. Greater than one-half but less than three-quarters. Greater than three-quarters, up to whole area. Score equals A x B x 5 Total maximum = 80 Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof), iris still | 2 |
| Opaque, iris invisible Area of Cornea Involved (B) One quarter (or less) but not zero Greater than one-quarter but less than one- half. Greater than one-half but less than three- quarters. Greater than three-quarters, up to whole area. Score equals A x B x 5 Total maximum = 80 Iris Values (A) Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof), iris still | 3 |
| One quarter (or less) but not zero Greater than one-quarter but less than one- half. Greater than one-half but less than three- quarters. Greater than three-quarters, up to whole area. Score equals A x B x 5 Total maximum = 80 Values (A) Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof), iris still | 4 |
| One quarter (or less) but not zero Greater than one-quarter but less than one- half. Greater than one-half but less than three- quarters. Greater than three-quarters, up to whole area. Score equals A x B x 5 Total maximum = 80 Values (A) Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof), iris still | - |
| Greater than one-quarter but less than one- half. Greater than one-half but less than three- quarters. Greater than three-quarters, up to whole area. Score equals A x B x 5 Total maximum = 80 Iris Values (A) Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof), iris still | |
| half. Greater than one-half but less than three- quarters. Greater than three-quarters, up to whole area. Score equals A x B x 5 Total maximum = 80 Iris Values (A) Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof), iris still | 1 |
| Greater than one-half but less than three- quarters. Greater than three-quarters, up to whole area. Score equals A x B x 5 Total maximum = 80 Iris Values (A) Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof), iris still | |
| quarters. Greater than three-quarters, up to whole area. Score equals A x B x 5 Total maximum = 80 Iris Values (A) Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof), iris still | 2 |
| Greater than three-quarters, up to whole area. Score equals A x B x 5 Total maximum = 80 Iris Values (A) Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof), iris still | |
| Score equals A x B x 5 Total maximum = 80 Iris Values (A) Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof), iris still | 3 |
| Score equals A x B x 5 Total maximum = 80 Values (A) Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof), iris still | • |
| Iris Values (A) Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof), iris still | 4 |
| Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof), iris still | |
| circumcorneal injection (any or all of these or combination of any thereof), iris still | . |
| circumcorneal injection (any or all of these or combination of any thereof), iris still | |
| or combination of any thereof), iris still | |
| | |
| | |
| - positive). | 1 |
| No reaction to light, hemorrhage, gross des- | |
| truction (any or all of these). | 2 |
| Score equals A x 5 Total maximum = 10 | |

TABLE II continued

Eye Irritation Test - Albino Rabbits

Scale of Weighted Scores for Grading the Severity of Ocular Lesions

| Ocular | | |
|-------------|---|----------|
| Tissues | Description · | Grading |
| Conjunctiva | Redness (A) | |
| | | |
| | Redness (refers to palpebral conjunctiva only). | |
| | Vessels definitely injected above normal. | 1 |
| | More diffuse, deeper crimson red, individual | |
| | vessels not easily discernible. | 2 |
| | Diffuse beefy red. | 3 |
| | | |
| | Chemosis (B) | |
| | Any swelling above normal (includes nictitating | |
| | membrane). | 1 |
| | Obvious swelling with partial eversion of the lids. | 2 |
| | Swelling with lids about half-closed. | 3 |
| | Swelling with lids about half-closed to completely | |
| | closed. | 4 |
| | | |
| | Discharge (C) | |
| | Any amount different from normal (does not in- | |
| | clude small amount observed in inner canthus | • |
| | of normal animals). | 1 |
| | Discharge with moistening of the lids and hairs | _ |
| | just adjacent to the lids. | 2 |
| | Discharge with moistening of the lids and hairs | <u> </u> |
| | and considerable area around eye. | 3 |
| | | • |
| | Score $(A + B + C) \times 2$ Total maximum = 20 | |

Note: The maximum total score is the sum of all scores obtained for the cornea, iris, and conjunctiva.

The rating is arrived at by selecting the maximum mean irritation score at one, 24 or 72 hours after instillation. If the rate of dissipation of injury does not meet the requirements defined for the descriptive rating appropriate for a particular numerical score, the descriptive rating is raised by one or more levels. The rating system is presented in Table III.

TABLE III

Eye Irritation Test - Albino Rabbits

Classification of Test Materials Based on Eye Irritation Properties

| Rating | Range | Definition |
|-------------------------------|--------------|---|
| Non-Irritating | 0.0 - 0.5 | To maintain this rating, all scores at the 24-hour reading must be zero; otherwise, increase rating one level. |
| Practically Non-Irritating | > 0.5 - 2.5 | To maintain this rating, all scores at the 24-hour reading must be zero; otherwise, increase rating one level. |
| Minimally Irritating | > 2.5 - 15.0 | To maintain this rating, all scores at the 72-hour reading must be zero; otherwise, increase rating one level. |
| Mildly Irritating | >15.0 - 25.0 | To maintain this rating, all scores at the 7-day reading must be zero; otherwise, increase rating one level. |
| Moderately Irritating | >25.0 - 50.0 | To maintain this rating, scores at 7 days must be < 10 for 60% or more of the animals. Also, mean 7-day score must be < 20. If 7-day mean score is < 20 but < 60% of animals show scores <10, then no animal among those showing scores > 10 can exceed a score of 30 if rating is to be maintained; otherwise, raise rating one level. |

TABLE III continued

Eye Irritation Test - Albino Rabbits

Classification of Test Materials Based on Eye Irritation Properties

| Rating | Range | . Definition |
|-------------------------|--------------|---|
| Severely Irritating | >50.0 - 80. | To maintain this rating, scores at 7 days must be ≤ 30 for 60% or more of the animals. Also, mean 7-day score must be ≤ 40. If 7-day mean score is ≤ 40 but <60% of the animals show scores ≤ 30, then no animal among those showing scores > 30 can exceed a score of 60 if rating is to be maintained; otherwise, raise rating one level. |
| Extremely Irritating | >80.0 - 110. | 0 |

C. Primary Skin Irritation Test - Albino Rabbits

Young albino rabbits of the New Zealand strain were used in the evaluation of the primary skin irritating properties of the test material.

The test procedure was modeled after that of Draize et al.*

Priof to the application of the test material, the hair was clipped from the back and flanks of each rabbit. Two test sites located lateral to the midline of the back approximately ten centimeters apart were selected. One of the two sites was abraded by making four epidermal incisions, two perpendicular to the other two, while the other test site remained intact.

Exactly 0.5 ml of undiluted test material (0.5 g of test material moistened with a minimum amount of water in the case of solids) was applied to each of the test sites on each rabbit. The test sites were immediately occluded with two-inch square gauze patches. The patches were placed directly over the test sites and secured with masking tape. The trunk of each animal was then wrapped with impervious plastic sheeting. The wrap held the patches in position and retarded evaporation of the test material during the 24-hour exposure period.

At-the end of 24 hours, the plastic wrappings and patches were removed. The intact and abraded test sites were examined and scored separately for erythema and edema on a graded scale of 0 to 4. After 72 hours, the sites were reexamined and rescored.

^{*} Draize, John H., Woodard, Geoffrey, and Calvery, Herbert O.,

"Methods for the Study of Irritation and Toxicity of Substances Applied
Topically to the Skin and Mucous Membranes," J. Pharm. & Exp. Ther.
82, 377 (1944).

In evaluating the average irritation present, the mean scores for erythema and edema of the intact test sites after 24 and 72 hours were added. Similarly, the mean scores for erythema and edema of the abraded test sites after 24 and 72 hours were added. These two values were totaled and divided by four to obtain the mean primary irritation score. The scoring criteria for erythema and edema are shown in Table IV.

The following grading system was used to arrive at a descriptive primary skin irritation rating:

| Mean Primary Irritation Score | | | |
|-------------------------------|-----------------------|--|--|
| (Range of Values) | Descriptive Rating | | |
| 0 | Non-Irritating | | |
| 0.1 - 0.5 | Minimally Irritating | | |
| 0.6 - 1.5 | Slightly Irritating | | |
| 1.6 - 3.0 | Mildly Irritating | | |
| 3.1 - 5.0 | Moderately Irritating | | |
| 5.1 - 6.5 | Severely Irritating | | |
| 6.6 - 8.0 | Extremely Irritating | | |

TABLE IV

Primary Skin Irritation Test - Albino Rabbits

Scoring Criteria for Skin Reactions

| Reaction | Description | Score |
|-----------------|---|-------|
| Erythema | Barely perceptible (Edges of area not defined) | 1 |
| • | Pale red in color and area definable | 2 |
| | Definite red in color and area well defined | 3 |
| | Beet or crimson red in color | 4 |
| Edema | Barely perceptible (Edges of area not defined) | . 1 |
| | Area definable but not raised more than 1 mm | 2 |
| | Area well defined and raised approximately 1 mm | 3 |
| | Area raised more than 1 mm | 4 |
| Injury in Depth | Escharosis, Necrosis | ₹ .8. |
| | Maximum Primary Irritation Score | = 8 |

IV. Results

- A. Acute Oral Toxicity Study Albino Rats
 - 1. Mortality and Body Weights

Individual mortality and body weight data are presented in Table V.

TABLE V

TEST MATERIAL: VARISOFT 222

Acute Oral Toxicity Study - Albino Rats

Mortality and Body Weight Data

| | Animal | Individual Body Weights | s (grams) | | |
|---------|---------|-------------------------|-----------|---------------------------------------|---------|
| Dose* | Number | Test Day Numbe | | Number Dead | Percent |
| (mg/kg) | and Sex | 0 | 14 | Number Tested | Dead |
| 10,250 | 1-M | 175 3 | 05 | 0/4 | • |
| | 2-M | | 99 | 0/4 | 0 |
| | 3-F | - * - | 215 | | |
| | 4-F | | 21 | | |
| 15,380 | 5-M | 165 2 | 198 | 0/4 | 0 |
| | 6-M | | 02 | 0/4 | 0 |
| | 7-F | - | 17 | | |
| | 8-F | | 24 | | |
| 23,070 | 9-M | 165 2 | 96 | 0/4 | 0 |
| | 10-M | | 10 | 0/4 | 0 |
| | 11-F | | 16 | | |
| | 12-F | | 29 | | |
| 34,600 | 13-M | 188 3 | 08 | 0/4 - | • |
| · | 14-M | - A . | 85 | 0/4 | 0 |
| | 15-F | _ | 12 | | |
| | 16-F | | 24 | • • • • • • • • • • • • • • • • • • • | ٠ |

Acute Oral $LD_{50} > 34,600 \text{ mg/kg}$

^{*} The test material was administered undiluted.

2. Reactions

The untoward reactions exhibited by the rats following oral administration of VARISOFT 222 included hypoactivity and ruffed fur (all dose levels). Onset of these reactions was noted within one hour after dosing. At the end of 24 hours all animals appeared normal.

Necropsy at sacrifice revealed no gross pathologic alterations among any of the animals.

B. Eye Irritation Test - Albino Rabbits

The results of the eye irritation test are presented in Table VI.

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TABLE VI

TEST MATERIAL: VARISOFT 222

| Rabbits |
|------------|
| Albino |
| Test - |
| Irritation |
| Eye |

Results

| | | | | | 1 | | |
|---------------------|--------|-----------|---------------|-------|-------|------|-------|
| | Rabbit | 1 | 1 | 24 | 72 | 7 | |
| Tissue | Number | Minute | Hour | Hours | Hours | Days | |
| Cornea (D-A) | | 0 | . 0 | 0 | 0 | 0 | vices |
| ris | | 0 | 0 | 0 | 0 | 0 | , - |
| Conjunctiva (R-S-D) | | 8 (2-0-2) | 10 (3-1-1), H | 0 | 0 | 0 | |
| Total | | 8 | 10 | 0 | 0 | 0 | |
| Cornea (D-A) | 7 | 0 | 0 | 0 | 0 | 0 | |
| ris | | 0 | 0 | 0 | 0 | 0 | |
| Conjunctiva (R-S-D) | | 8 (1-1-2) | 8 (1-1-2) | 0 | 0 | 0 | 1 |
| [otal | | 8 | 8 | 0 . | 0 | 0 | |
| Cornea (D-A) | ٣ | 0 | 0 | 0 | 0 | 0 | |
| SIL | | 0 | ΙŃ | 0 | ò | 0 | |
| Conjunctiva (R-S-D) | | 4 (1-0-1) | 12 (2-2-2) | 0 | 0 | 0 | 1 |
| Total | | 4 | 17 | 0 | 0 | 0 | t . |
| Cornea (D-A) | 4 | 0 | 0 | 0 | 0 | 0 | |
| 118 | | 0 | 0 | 0 | 0 | 0 | |
| Conjunctiva (R-S-D) | | 4 (1-0-1) | 8 (1-1-2) | 0 | 0 | 0 | į |
| Total | | 4 | 8 | 0 | 0 | 0 | |
| | | | | | | | |
| | | | | | | | 1 |

BEST COPY AVAILABLE

TABLE VI continued

TEST MATERIAL: VARISOFT 222

Eye Irritation Test - Albino Rabbits

Results

| | Rabbit | 1 | | 24 | 72 | 7 | ı |
|---|--------|--|-----------------------|---|----------------------------|--------------------|---|
| Fissue | Number | Minute | Hour | Hours | Hours | Days | |
| Cornea (D-A) | 5 | 0 0 | . 0 15 | 0 0 | 0 0 | 0 0 | |
| Conjunctiva (R-S-D) Total | | 8 (1-1-2) 8 | 10 (2-1-2) | 0 | 0 | 0 | |
| Cornea (D-A) ris | 9 | 0 0 4 (1-0-1) | 0 5 8 (2-1-1) | 000 | 000 | 0 0 0 | |
| Fotal | | 1 | 13 | 0 | 0 | 0 | |
| Averages Cornea ris Conjunctiva | | 0.0 0.0 6.0 | 0.0 2.5 9.3 | 0.0 | 0.0 | 0.0 0.0 | - |
| [ota] | | 9.0 | 11.8 | 0.0 | 0.0 | 0.0 | |
| Sornea:) = Density) = Area Sorneal Score = D x A x 5 Saximum Score = 80 | ς × 5 | <u>Iris:</u> Iris Score = Value x 5 Maximum Score = 10 | Value x 5 ore = 10 | Conjunctiva: R = Redness S = Swelling D = Discharge Conjunctival Score = (R+S+D) x 2 Maximum Score = 20 | H = Нето 72 72 72 | = Hemorrhages 24 7 | 1 |

C. Primary Skin Irritation Test - Albino Rabbits

The results of the primary skin irritation test are presented in Table VII.

TABLE VII
TEST MATERIAL: VARISOFT 222

Primary Skin Irritation Test - Albino Rabbits

Results

| | Irritati | | es for . ites At: | Abraded | Irritati | ion Scor Skin Sit | | ntact |
|----------|----------|------|----------------------|---------|----------|----------------------|------|-------|
| Animal | 24 H | ours | 72 F | lours | 24 H | ours | 72 H | ours |
| Number | Er. | Ed. | Er. | Ed. | Er. | Ed. | Er. | Ed. |
| 1 | 2 | 1 | 2 | 0, D | 2 | 0 | 2 | 0, D |
| 2 | 2 | 1 | 2 | 0, D | 2 | 0 | 2 | 0, D |
| 3 | 1 | 0 | 1 | 0 | 1 | 0 | 1 | 0 |
| 4 | 2 | 1 | 2 | 0, D | 2 | 0 | 2 | 0, D |
| 5 | 2 | 0 | 2 | 0 | 2 | 0 | 2 . | 0 |
| 6 | 2 | 0 | 2 | 0 | 2 | 0 | 2 | 0 |
| Mean | 1.8 | 0.5 | 1.8 | 0.0 | 1.8 | 0.0 | 1.8 | 0.0 |
| Subtotal | | 4. | 1 | | | 3. | 6 | _ |

Primary Irritation Score = 1.9

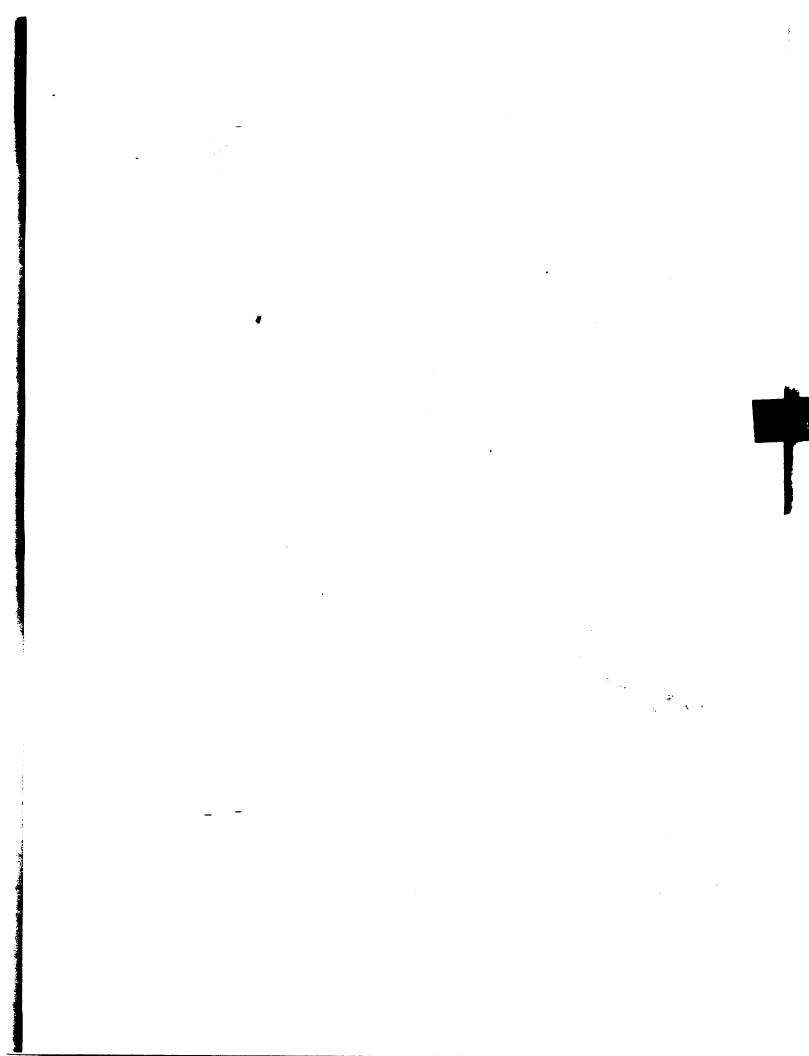
Key:

Er. = Erythema

Ed. = Edema

D = Desquamation

. -



Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to
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Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

Attachment 12:

Rosner-Hixson Laboratories Report - Acute LD50 [PEQ 68410-69-5, 18% dispersion]

ROSKER-HIXSON LABORATORIES

7737 South Chicago Avenue/Chicago, Illinois 60619/Area Code 312 REgent 4-0142



REPORT Laboratory No. PT68-7

Oral LDSO 18% 222

CLIENT:

Northern Petrochemical Company of Janesville, Wisconsin.

SAMPLE:

Softener 1210 (18% Dispersion of V.222)

OBJECT:

To determine the LD₅₀ with special reference to the requirements of the Federal Hazardous Substances Labeling Act.

EXPERIMENTAL AND RESULTS:

Single Oral Doses

The product was diluted 1+1 with 1,2 propanediol employing gentle warming. Ten ml per kg of diluted sample was administered to eight Sprague-Dawley rats previously fasted overnight, and weighing 320 to 395 gm. The oral administration was made by using a syringe with a modified 17 gauge hypodermic agrile.

The animals were closely observed following dosing and over a subsequent 14 day observation period, at the conclusion of which they were weighed, sacrificed and subject to a gross autopsy.

All animals survived the 14 day period. On autopsy livers and kidney cortices were darker than usual.

Table 1 gives the initial and final weights of the animals employed

CONCLUSION:

The LD of Northern Petrochemical Company's Softner 1210 was found to be greater than 5 ml/kg. On this basis the test sample meets the requirements of the Federal Hazardous Substances Labeling Act.

September 9, 1968

ROSNER-HIXSON LABORATORIES

Phillip S. Wuke Phillip S. Duke, Ph.D.

Assistant Technical Director



TABLE 1

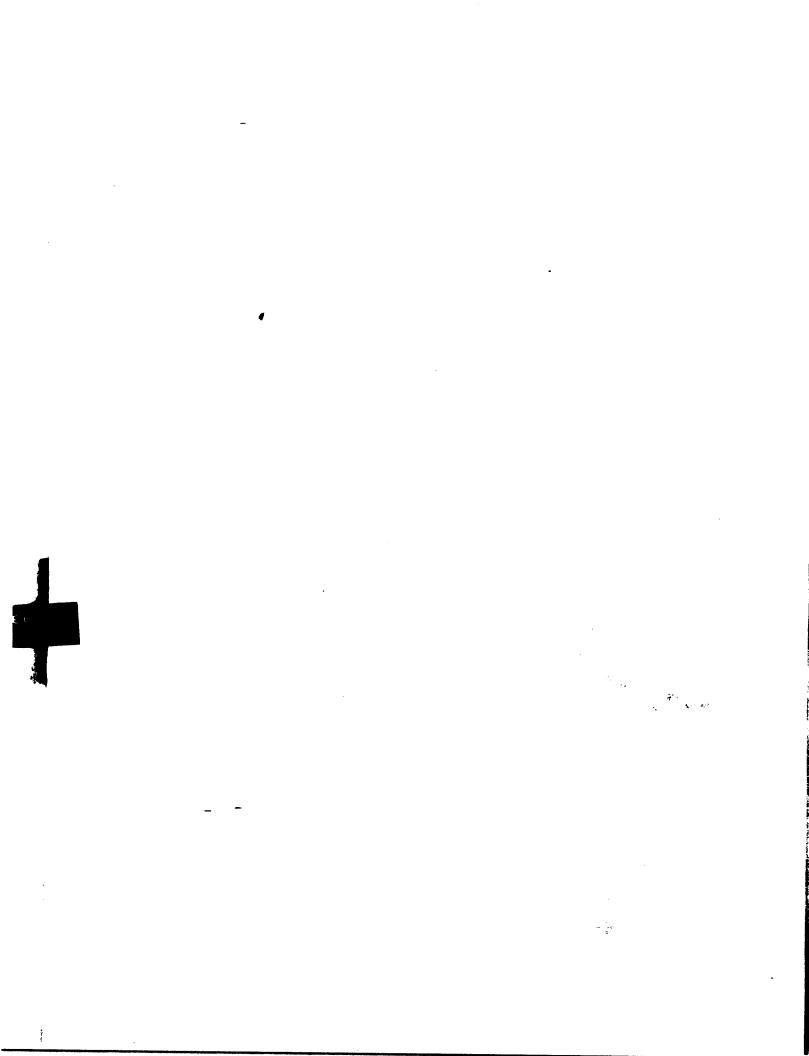
ACUTE RAT ORAL TOXICITY

SAMPLE: SOFTENER 1210

SAMPLE ADMINISTERED DILUTED 1 + 1 WITH 1,2 PROPANEDIOL

| Animal Number | Body Weight grams | Weight After 14 Days grams | Dose of Diluted Sample | Dosage of Undiluted Sample ml/kg | Days to Death |
|------------------|-------------------------|----------------------------------|------------------------|--|------------------|
| 9 | 330 | 363 | 3.3 | • | 0 |
| 10 | 320 | 369 | 3.2 | , , | Survived |
| 11 | 320 | 364 | | 3 | Survived |
| | | | 3.2 | 5 | Survived |
| 12 | 337 | 378 | 3.4 | 5 | Survived |
| 13 | 331 | 375 | 3.3 | Ē | |
| 14 | 395 | 458 | | 2 | Survived |
| 15 | | | 4.0 | 5 | Survived |
| | 340 | 392 | 3.4 | 5 | Survived |
| 16 | 325 | 384 | 3.2 | 5 | Survived |

The acute rat oral LD of sample was found to be greater than 5 ml/kg



Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

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Attachment 13:

WARF Institute Report 7117554 - Primary Eye Irritation [PEQ 68410-69-5]

MADISON, WISCONSIN

Reports are submitted to clients on a confidential basis. No reference to the work, the results or to the Institute in any of advertising, news release or other public announcement may be made without written authorization from the Inst

REPORT

Analysis for

Primary Eye Irritation

Description of Sample

Variout 222 - 907

Date Received

11-16-77

Reference Number

644750

Submitted by

Richard M. Igan

Ashland Chemical Co.

Dublin, OH

Claimed Content

Results

Rye Irritation Searce: 24 Hr. 48 Hr. 72 Hr. 7 Day 14 Day 7 Test

Method

Please see the attached protocol.

Remarks

by and for the

WARF INSTITUTE, INC.

Date

December 21, 1977

WARF Institute No.

7117554



MADISON, WISCONSIN

ETE IRRITATION

Client Ashlend Chemical Co.

WARF Institute No. 7117554

Sample Varisoft 222 - 90% 644750

Test Animal: Young adult rabbits (approximately 14 weeks of age) of the New Zeeland white strain weighing 2.5 to 3.5 kg were procured, naintained individually in screen bottom cages in air conditioned quarters, provided continuous access to commercial laboratory feed and water and hald for a conditioning period of at least 7 days.

<u>Method</u>: Conditioned saimals were chosen at random, treated and maintained as specified for the conditioning period.

For each animal treated, one-tenth of a milliliter (0.1 gm for solids) of the test substance was instilled into one eye and the untreated eye served as a control. The reaction to the test natural was read according to the scale of seering for damage at specified times after instillation. Any residue of the test unterial and accumulated discharge were flushed from the eyes each time they were secred.

Concentration of Test Sample: as submitted

Special Washing: nome

Results:

| | Rabbit Humber | Corne Opacity | Area | Iris | Rodness | <u>Chancels</u> | <u>Discharge</u> |
|------|------------------|------------------|-------|-----------|----------|-----------------|--|
| | 133 | 1 | 4 | 0 | 2 | 3 | 2 |
| | 134 | <u> </u> | ò | ŏ | 2 | 2 | 2 |
| 24 | 135 | Ö | Ŏ | Ŏ | 2 | ī | 2 . |
| Hour | 136 | 0 | Ŏ | ŏ | 2 | 2 | i |
| | 137 | 0 | 0 | Ö | 2 | ī | 2 |
| | 138 | 0 | 0 | • | 2 | 2 | 2 |
| | | | Bye I | rritatio | a Secre: | 14.7 | - 4 15 - 1 15 - |
| | 133 | 0 | 0 | 0 | 2 | 2 | 2 |
| | 134 | 0 | 0 | Ō | 2 | ī | ī |
| 48 | 135 | 0 | 0 | 0 | 2 | ō | ō |
| Lour | 136 | 0 | 0 | 0 | 2 | 2 | ĭ |
| | 137 | 0 | 0 | 0 | 2 | Ō | ī |
| | _138_ | 0 | 0 | 0 | 2 | 2 | ī |
| | | | Eye I | rritation | a Score: | 8.3 | • |
| | 133 | 0 | 0 | 0 | 2 | 1 | 1 |
| | 134 | 0 | 0 | 0 | 2 | Ō | Ō |
| 72 | 135 | 0 | 0 | 0 | 1 | 0 | Ö |
| Hour | 136 | 0 | 0 | 0 | 2 | 1 | 0 |
| | 137 | ٥ | 0 | 0 | 1 | 0 | 0 |
| | 138 | 0 | 0 | 0 | 1 | 1 | 0 |

Rye Irritation Searce: 4.3

MADISON, WISCONSIN

ETE IRRITATION (CONTINUED)

Client Ashland Chemical Co.

WARF Institute No. 7117554

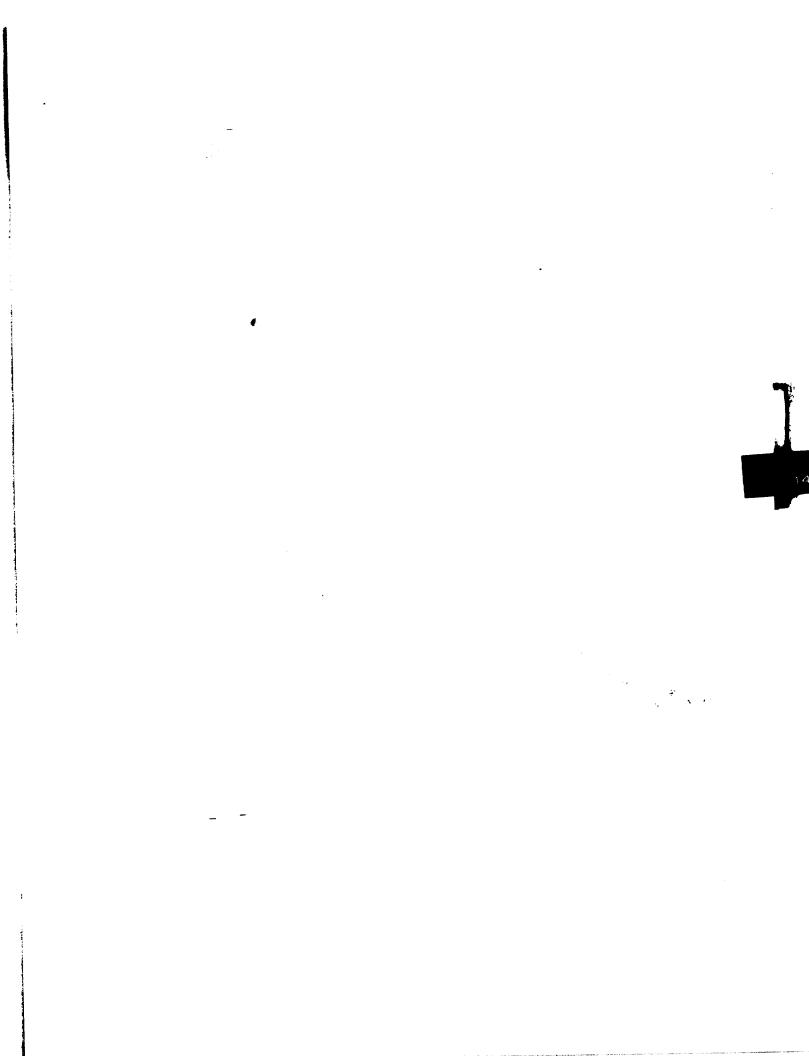
Sample Varisoft 222 - 90% 644750

Results:

| | Rabbit | Corne | | | | onjunctive | • |
|-----|--------|---------|------|----------|------------|------------|-----------|
| | Mumber | Opacity | Area | Iris | Redness | Chancels | Discharge |
| | 133 | *DOT | | | | . — | |
| | 134 | 0 | 0 | 0 | 2 | 1 | ۵ |
| 7 | 135 | 0 | a · | ۵ | Ō | 7 | Ŏ |
| Day | 136 | Ď | Ŏ | ŏ | • | • | 0 |
| | 137 | 1 0 | ŏ | • | Č | • | |
| | | • | _ | Ō | v | ¥ | 0 |
| | 138 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | | ye Irrib | stion Soor | e: 1.0 | |
| | 133 | *901 | | | | _ | |
| | 134 | *BOT | | | | - | _ |
| 14 | 135 | 0 | 0 | Q | ۵ | • | • |
| Day | 136 | ٥ | ā | ă | ŏ | | • |
| • | 137 | Ŏ | Ŏ | ŏ | • | • | 9 |
| | 138 | ŏ | Ž | V | U | U | U |
| | 136 | U | U | 0 | 0 | 0 | 0 |

Eye Irritation Score: 0

^{*}The animals that died on test did not appear to be test related.



Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

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Attachment 14:

1

Rosner-Hixson Laboratories Report - Eye Irritation [PEQ 68410-69-5, 15% dispersion]

HIXSON LABORATORIES

Telephone Chicago Avenue/Chicago, Illinois 60619/Area Code 312 REgent 4-0142



Laboratory No. 15% 222

Northern Petrochemical Company of Das Plaines, Illinois. CLIENT:

Varisoft 222, Aqueous Dispersion at 15% Solids Level. SAMPLE:

To determine eye irritation potential in accordance with Federal OBJECT:

Hazardous Substances Labeling Act Regulations.

EXPERIMENTAL & RESULTS:

The eye irritation properties of sample were tested by instilling 0.1 milliliter into the right eye of each of nine rabbits, the left eye remaining untreated to serve as control.

> eyes unwashed. Rabbits 1-6:

30 seconds after treatment Rabbits 7-9:

eyes washed with 20 milliliters

of water.

Observations of ocular lesions were made on the rabbits' eyes after 24, 48, 72, 96 and 168 hours. At these intervals the extent and degree of irritation were scored. The general technic of evaluation and scoring followed the recommendations of J.H. Draise, G. Wooderd and H. O. Calvery, Journal of Phermacology and Experimental Therapeutics, vol. 82, pg. 377 (1944) and Sec. 191.12 of Federal Hazardous Substances Labeling Act Regulations Guide for Grading Eye Irritation. Fluorescein sodium and ultraviolet light illumination were used to determine extent and degree of irritation. The scores obtained are shown in Table 1:

In rabbits with unwashed eyes, one rabbit showed a grade 1 conjunctival erythems which was normal at 48 hours after treatment. Rabbits with washed eyes showed no eye irritation reaction.

SURGIARY & CONCLUSION:

Varisoft 222, Aqueous Dispersion at 15% Solids Level, was tested for eye irritation in accordance with Federal Hazardous Substances Labeling Act Regulations.

Instillation of sample in eyes of rabbits did not produce a positive eye irritation reaction according to Federal Hazardous Substances Labeling Act Regulations.

On this basis, the sample is not an eye irritant and does not require any precautionary labeling.

LABORATORIES

Technical Director

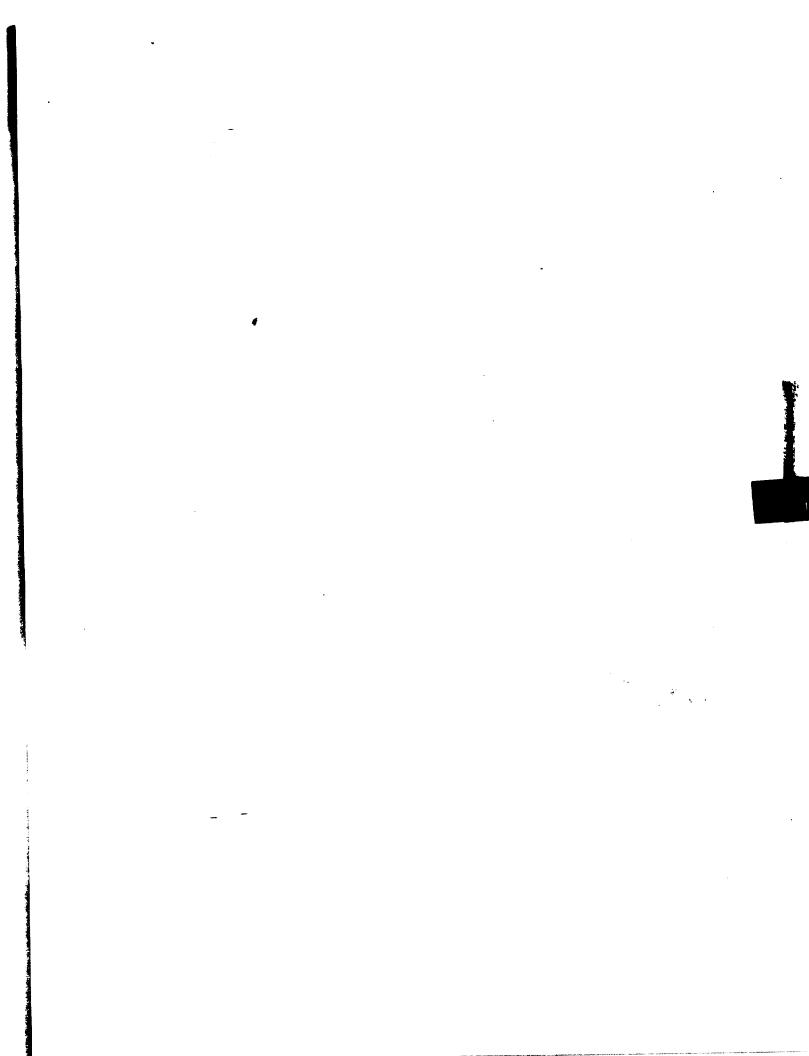
May 18, 1971

TABLE 1

RABBIT EYE IRRITATION

SAMPLE: VARISOFT 222. AQUEOUS DISPERSION AT 15% SOLIDS LEVEL

| Rabbit Number | • | | | 1 | | | | | 2 | | | | | 3_ | | |
|-----------------|-------------|------------|-----------|-----------|-----------|------------|------------|----|-----------|-----------|-------------|-----------|------|-----------|-----------|-----------------|
| Hours After Tre | na tmant | 24 | 48 | 72 | 96 | 168 | 24 | 48 | 72 | 96 | 168 | 24 | 48 | <u>72</u> | <u>96</u> | 168 |
| Cornea | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Iris | Parent home | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 |
| Conjunctives: | Erythema | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| | Chemosis | U | U | J | Ū | J | J | | | • | · | - | | | | |
| | | | | | | | | | e | | | | | 4 | | |
| Rabbit Number | | | | 4 | | | | | | ~ | 1/0 | | /. 0 | <u></u> | 06 | 168 |
| Hours After Tr | estment | <u>24</u> | 48 | <u>72</u> | <u>96</u> | <u>168</u> | <u>24</u> | 48 | <u>72</u> | <u>96</u> | <u>168</u> | 24 | 48 | <u>72</u> | <u>96</u> | <u>168</u> 0 |
| Cornea | | 0 | Ò | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | _ |
| Iris | | 0 | v | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Conjunctiveet | Erythems | 0 | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 9 | 0 | 0 | 0 | 0 | 0 | 0 |
| | Champeis | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | | | | | | | | | | | | | | |
| Rabbit Number | | | | 7 | | | | | 8 | | | | | 9 | | |
| Hours After Tr | reatment | <u> 24</u> | <u>48</u> | <u>72</u> | <u>96</u> | 168 | <u> 24</u> | 48 | <u>72</u> | <u>96</u> | <u> 168</u> | <u>24</u> | 48 | 72 | <u>96</u> | 168 |
| Cornes | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Iris | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Conjunctivae: | Erythema | 0 | υ | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | Chemosis | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | _ | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | |



Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated February 22, 1993 from Dr. John D. Walker, Executive Director, TSCA Interagency Testing Committee, to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to Data Submissions from QUATS Steering Committee Members Filed in Response to the 22nd Report of the TSCA Interagency Testing Committee

Attachment 15:

Rosner-Hixson laboratories Report - Skin Irritation [PEQ 68410-69-5, 4% dispersion]



6/10/10

Dermal Fritation

PT64-

CLIENT: Varney Chemical Company of Janesville, Wisconsin.

SAMPLE: Two containers labeled Arqued 2HT (4% Dispersion) and Varisoft

222 (4% Dispersion) were received in our laboratory on May 25,

1964.

OBJECT: To determine the skin irritation potential of the subject

materials by repeated application to the skin of rabbits.

METHODS: A modification of the technique described by Draize, et al.

8: A modification of the technique described by Draize, et al (1) was used to study the effects of repeated applications to the products. The hair was clipped from the abdomen of six male albino rabbits, and four areas on the abdomen, approximately ten centimeters apart were designated for application of the products. Two areas on each side of the ventral mid-line were abraded by making four epidermal incisions (two perpendicular to two others in the area of the site) with the point of a 21 gauge needle. The sites were randomized for application of the products to both the intact and abraded sites.

Application of Sample

One-half milliliter of the respective samples was placed on a small square of cotton gauze and maintained in contact with the skin under a larger square of polyethylene film and anchored to the skin with strips of adhesive tape. A square of flammal cloth was then taped around the trunk of the animal to further protect the patches from being dislodged.

After 24 hours the vest and patches were removed and the skin examined for signs of irritation (erythems and/or edems). Examination was made again after 72 hours. The application of the sample was renewed at 72 hours and each subsequent working day for a total of eight applications. Since the patches were not removed on weekends this resulted in a total of twelve days of contact of the products with the skin.

A. 250

RESULTS: The initial 24 hour, 72 hour, and 2 week irritation scores are presented in Tables 1 and 2. The primary irritation index for Arquad 2HT, 4% Dispersion, was calculated to be 1.39 and for Varisoft 222, 4% Dispersion, 1.47. Examination of the skin two weeks after the initial application indicated that no significant irritation was present in the case of Arquad 2HT, whereas in the case of Varisoft 222 a minimal degree of erythems and edems was present.

CONCLUSION:

'Arquad 2HT and Varisoft 222 when applied as 4% Dispersions repeatedly over a two week period to rabbit skin were found to produce only a minimal degree of skin irritation.

June 10, 1964

ROSMER-HIXSON LABORATORIES

Bob West, Ph.D. Assistant Director

TABLE 1

SKIN INDITATION SCORES

ARQUAD 2HT. 4% DISPERSION

UNARRADED SITES

| | 24 Hous | ' a | 72 Hou | T 8 | Two We | eks |
|------------------|------------|------------|----------|------------|----------|-------|
| Rabbit Number | | dema | | Edema | Erythema | Edems |
| | 2 | 1 | 0 | 0 . | 0 | 0 |
| H1410 | 1 | ī | 0 | 0. | 0 | 0 |
| H1411 | <u>.</u> | 1 | ĭ | 1 | 0 | 0 |
| H1412 | <u>.</u> | <u>.</u> | • | ā | ă | 0 |
| H1413 | 1 4 2 | 1 | 0 | 0 | Õ | Ŏ |
| . н1414 | 2 | 1 | 0 | Ŏ | Õ | Ü, |
| H1415 | O . | 0 | 0 | 0 | • | • |
| , | Average: | 2.17 | yverage: | 0.34 | Average: | 0 |
| | • | | ARRADE | SITES | | |
| , , | • | 1 | 0 - | 0 | 0 | 0 |
| H1410 | • | ī | Ď | ۵ | 0 | ð |
| H1411 | <u>.</u> | • | ĭ | ĭ | 0 | 0 |
| H1412 | 1 | ı. | • | à | Ŏ | Ō |
| H1413 | 2 | 2 | Ų | 0 | Ŏ | Ŏ |
| H1414 | 2 | 1 | 0 | V | 0 | Ŏ. |
| H1415 | 1 | 1 | 0 | Ü | U | . ^ |
| 44-7 | Average: | 2.67 | Average: | 0.34 | Average | ; 0 |

TABLE 2

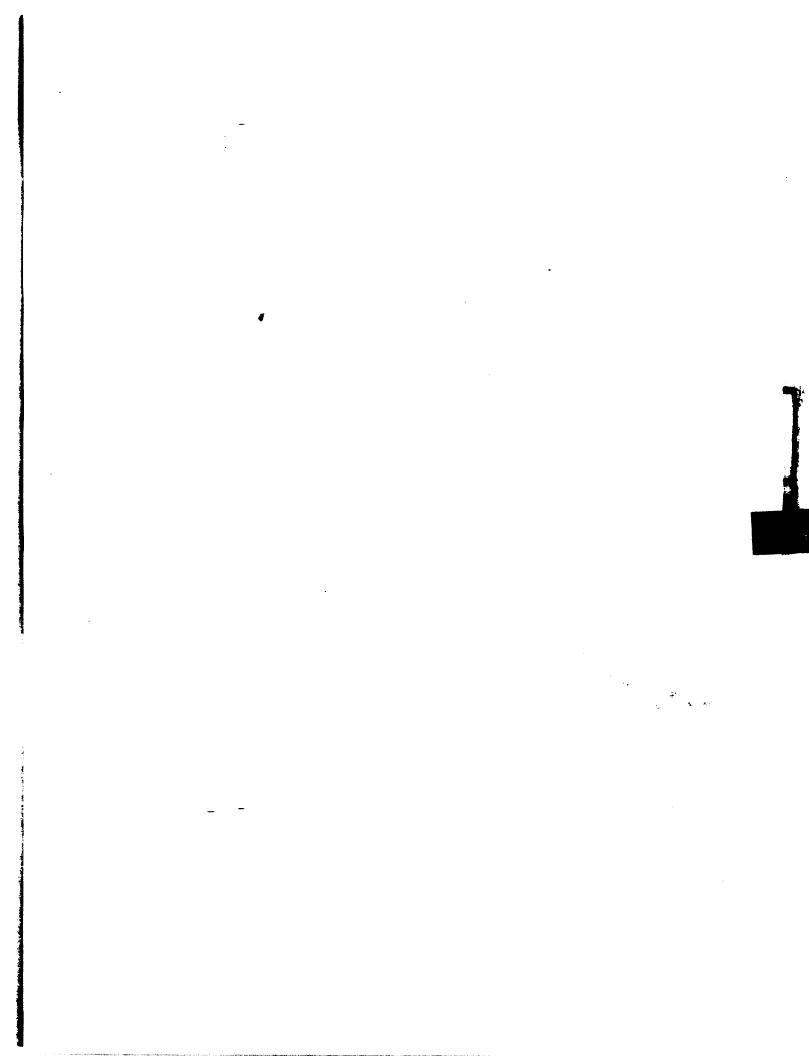
SKIN IRRITATION SCORES

VARISOFT 222. 4% DISPERSION

IMARRADED SITES

| | - | | The second second | | | |
|--|--------------------------------|-----------------|--|-----------|--|-------------------------------|
| Rabbit | 24 Ho | Rdems. | 72 Hos | Edema | Two We | Edema |
| Hupber H1410 H1411 H1412 H1413 H1414 H1415 | Erythema 1 1 2 - 1 2 Average: | 1 0 1 1 1 1 1 1 | 0 0 0 0 1 0 Average: | 0 0 0 0 1 | 1 2 2 0 0 2 Average: | 1 1 0 0 1 1.17 |
| | | | | | | |

| H1410 | 2 | 1 | 1 | 0 . | 1 | 1 |
|-------|------------|------|----------|------|----------|------|
| H1411 | . <u>1</u> | 1 | 0 | 0 | | • |
| | · ī | 1 | 0 | 0 | 1 | ŗ |
| H1412 | 2 | 2 | 0 | 0 | 0 | 0 |
| H1413 | • | 7 | 2 | 1 | 1 | 1. |
| H1414 | <u>L</u> | | • | 0 | 2 | 1. |
| H1415 | 2 | 2 67 | Average: | 0.67 | Average: | 1.83 |



Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

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Attachment 16:

Report to Northern Petrochemical Company Primary Skin Irritation of Eight Samples of Shampoo
in Albino Rabbits
[PEQ 68410-69-5, Full strength and 4% dispersion]

real? Irritation 8%

REPORT TO

NORTHERN PETROCHEMICAL COMPANY

PRIMARY SKIN IRRITATION TESTS WITH EIGHT SAMPLES OF SHAMPOO IN ALBINO RABBITS

P.O. NO. 54941

MARCH 13, 1972

IBT NO. A1249

I. Introduction

At the request of Northern Petrochemical Company, a primary skin irritation test was conducted with each of eight samples of shampoo. The samples were identified as:

- A.

Varisoft 222

- 2. 8% Dispersion of Varisoft 222 in water
 - 3. Varisoft 475
 - 4. 8% Dispersion of Varisoft 475 in water
 - 5. Varisoft 100
 - 6. 8% Dispersion of Varisoft 100 in water
 - 7. 10% Active Varion CADG in water
 - 8. 10% Active Tegobetainec in water

II. Summary

The results of the rabbit primary skin irritation tests with eight samples of shampoo are summarized in Table I.

Respectfully submitted,

INDUSTRIAL BIO-TEST LABORATORIES, INC.

Report prepared by:

Kenneth Ebbens, B.S. Assistant Toxicologist

Acute Toxicity

Report approved by:

Carmen Mastri, B.S. Senior Group Leader Acute Toxicity

Manager, Toxicology

bb

TABLE I
Summary of Results

| _ | Mean Primary | |
|--|------------------|-----------------------|
| Test Material | Irritation Score | Results |
| Varisoft 222 | 8.0/8.0 | Extremely Irritating* |
| 8% Dispersion of Varisoft 222 in water | 6.0/8.0 | Severely Irritating* |
| Varisoft 475 | 8.0/8.0 | Extremely Irritating* |
| 8% Dispersion of Varisoft 475 in water | 5.1/8.0 | Severely Irritating* |
| Varisoft 100 | 5.6/8.0 | Severely Irritating |
| 8% Dispersion of Varisoft 100 in water | 2.8/8.0 | Mildly Irritating |
| 10% Active Varion CADG in water | 3.3/8.0 | Moderately Irritating |
| 10% Active Tegobetainec in water | 3.4/8.0 | Moderately Irritating |

^{*} The chemical burns were superficial and considered not to result in fibrotic tissue replacement.

III. Investigational Procedure

Twelve young albino rabbits of the New Zealand strain were used in the evaluation of the primary skin irritating properties of the test material.

Prior to the application of the test material, the hair was clipped from the back and flanks of each rabbit. Four intact test sites located lateral to the midline of the back approximately ten centimeters apart were selected on each rabbit.

Exactly 0.5 ml of Varisoft 222, 8% Dispersion of Varisoft 222 in water, Varisoft 475 or 8% Dispersion of Varisoft 475 in water was applied to one of the four test sites on six of the rabbits. Varisoft 100, 8% Dispersion of Varisoft 100 in water, 10% Active Varion CADG in water and 10% Active Tegobetainec in water were applied in the same manner to the six remaining rabbits. The test materials were allowed to contact the skin for 24 hours. The sites remained unoccluded during the entire 24-hour contact period.

At the end of the 24-hour contact period the test sites were examined and scored separately for erythema and edema on a graded scale of 0 to 4. After 72 hours, the sites were reexamined and rescored.

In evaluating the average irritation present for each test material the mean scores for erythema and edema of the intact test sites after 24 and 72 hours were added. This score was divided by two to obtain the mean primary irritation score. The scoring criteria for erythema and edema are shown in Table II.

The following grading system was used to arrive at a descriptive primary skin irritation rating:

| ${\tt Mean}$ | Primary | Irritation | Score |
|--------------|-----------|------------|-------|
| | _(Range o | of Values) | |

0 0.1 - 0.5 0.6 - 1.5 1.6 - 3.0 3.1 - 5.0 5.1 - 6.5 6.6 - 8.0

Descriptive Rating

Non-Irritating
Minimally Irritating
Slightly Irritating
Mildly Irritating
Moderately Irritating
Severely Irritating
Extremely Irritating

TABLE II

Primary Skin Irritation Test - Albino Rabbits

Scoring Criteria for Skin Reactions

| Reaction | Description | Score |
|-----------------|---|----------|
| Erythema | Barely perceptible (Edges of area not defined) | 1 |
| | Pale red in color and area definable | 2 |
| | Definite red in color and area well defined | 3 |
| | Beet or crimson red in color | 4 |
| Edema | Barely perceptible (Edges of area not defined) | 1 |
| | Area definable but not raised more than 1 mm | 2 |
| | Area well defined and raised approximately 1 mm | 3 . |
| | Area raised more than 1 mm | 4 |
| Injury in Depth | Escharosis, Necrosis | 8 |
| | Maximum Primary Irritation Score = | 8 |

IV. Results _

The results of the primary skin irritation tests are presented in Tables III through X.

4

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TABLE III

TEST MATERIAL: Varisoft 222

Primary Skin Irritation Test - Albino Rabbits

Results - Unoccluded Test Sites

| | | | | on Scores for Intact | |
|----------|---|------|----------|----------------------|-------|
| | | | | kin Sites at: | |
| Animal | | 24 H | 24 Hours | | Hours |
| Number | - | Er. | Ed. | Er. | Ed. |
| 1 | | 4 | 4* | 4 | 4** |
| 2 | | 4 | 4* | 4 | 4** |
| 3 | | 4 | 4* | 4 | 4** |
| 4 | | 4 | 4* | 4 | 4** |
| 5 | | 4 | 4* | 4 | 4** |
| 6 | | 4 | 4* | 4 | 4** |
| Mean | | 4.0 | 4.0 | 4.0 | 4.0 |
| Subtotal | | • | | 16.0 | |

Key:

Er. = Erythema Ed. = Edema

** Escharosis

^{*} Superficial chemical burns over entire site

TABLE IV

TEST MATERIAL: 8% Dispersion of Varisoft 222 in water

Primary Skin Irritation Test - Albino Rabbits

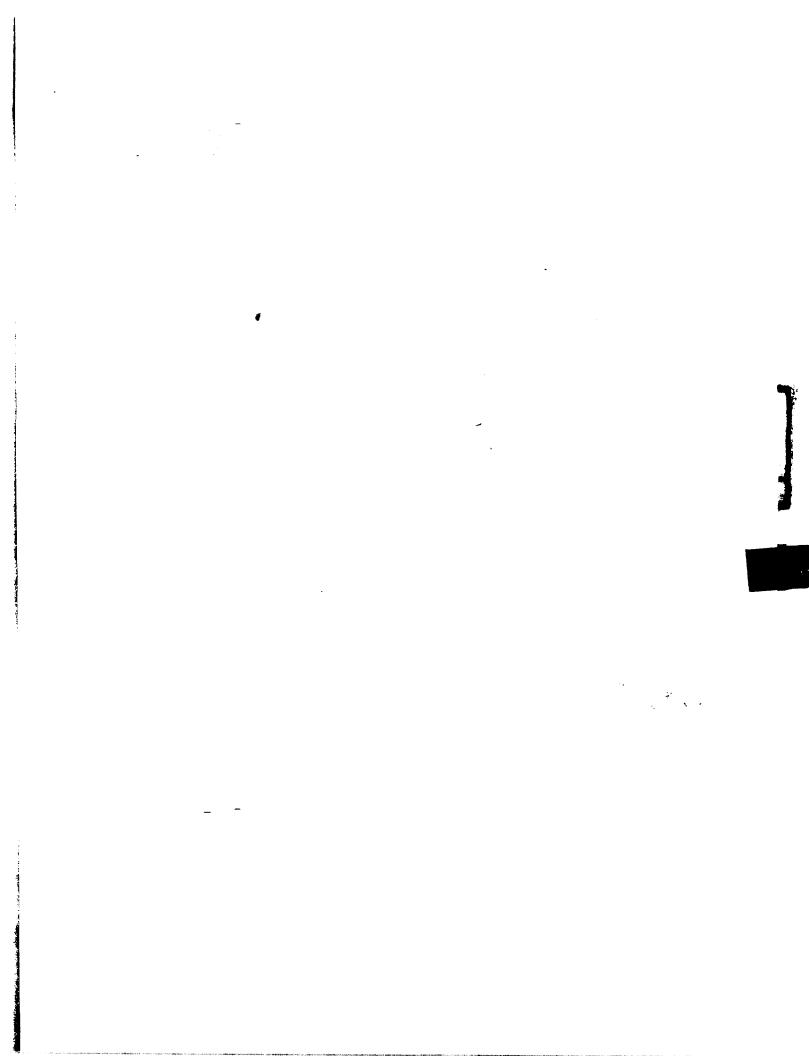
Results - Unoccluded Test Sites

| | Irritation Scores for Intact Skin Sites at: | | | | | |
|----------|---|--------------|------|------|--|--|
| Animal | 24 Hours | | | ours | | |
| Number | Er. | Ed. | Er. | Ed. | | |
| 1 | 2 | 1 | 2 | 0 | | |
| 2 | 4 | 4* | 4 | 4* | | |
| 3 | 4 | 4* | 4 | 4* | | |
| 4 | 2 | 2 | 2 | 2 | | |
| 5 | 3 | 2 | 3 | 2 | | |
| 6 | 4 | · 4 * | 4 | 4* | | |
| Mean | 3.2 | 2.8 | 3.2 | 2.7 | | |
| Subtotal | · | | 11.9 | | | |

Key:

Er. = Erythema Ed. = Edema

^{*} Superficial chemical burns



Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

Attachment 17:

Bio-Toxicology Laboratories Report DOT and FSHA Skin Irritation
[PEQ 68410-69-5]

Bio-Toxicology Laboratories, Inc.

Twin Oak Farm Division

Creek & Cox Roads, P. O. Box 267. Moorestown, N. J. 08057

Phone: (609) 665-1776 — 235-2908

January 21, 1974

Dr. N.S. Salomons
Ashland Chemical Company
P.O. Box 2219
Columbus, Ohio 48216

FSHA

Dear Dr. Salomons:

Following are the results of the experimental procedures conducted for Ashland Chemical Company.

MATERIAL:

Varisoft 222 - 90%

Varisoft 110

Varanol SLES-60%

Varanol SLES-30%

Varanol SLS

Varion 1017

RECEIVED:

January 17, 1974

EXPERIMENTAL PERIOD:

January 18 - Fanuary 21, 1974

EXPERIMENTAL PROCEDURES:

Primary Irritation Study

The conclusions in this study are based upon the results of the study completed January 21, 1974.

This report is submitted for the exclusive use of Ashland Chemical Company.

Very truly yours,

John Davis Paul

President

JDP/lsd



Department of Transportation Act

Varisoft 222-90%
Varisoft 110
Varonol SLES-60%
Varonol SLES-30%
Varonol SLS
Varion 1017

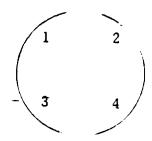
METHOD FOR PRIMARY IRRITATION

DEPARTMENT OF TRANSPORTATION ACT

The intact and abraded skin of 36 albino rabbits was employed for this study. A series of 6 rabbits was used for testing each substance. The hair was clipped from the backs with the aid of angora clippers. Four areas of the back, placed approximately ten centimeters apart, were designated for the positions of the patches. Areas 2 and 3 were abraded by making four epidermal incisions (two perpendicular to two others in the area of the patch). The patches consisted of 1.5 inch x 1.5 inch 12 ply gauze squares. The patches were secured to the area by thin bands of adhesive tape. The material to be tested (0.5 ml. for liquids and 0.5 gm. for solids) was introduced beneath the patch. The entire trunks of the animals were then wrapped in clear plastic trunk bands. The trunk bands help to hold the patches in position and retard evaporation of volatile substances during the four hour exposure period. Upon removal of the patches the resulting reactions were evaluated on the basis of weighted scores.

Following this initial reading, all test sites were washed with appropriate solvent to prevent further exposure. Readings were again made at 24 and 48 hours after the initial application. Each test substance is evaluated on a total of site (6 abraded and 6 intact).

The primary irritation index is calculated by adding the values for erythema or eschar formation, and edema at 4, 24 and 48 hours on intact and abraded skin (12 values) and dividing by six to obtain an individual score on each rabbit.



2 and 3 = abraded

1 and 4 = intact

l and 2 = control (if employed)

3 and 4 = test material

METHOD OF POINT SCORING

FOR

EVALUATION OF SKIN REACTIONS

| Α. | Erythema and Eschar Formation Very slight erythema (barely perconduction) Well defined erythema Moderate to severe erythema Severe erythema (beet redness) to (injuries in depth) | | 1 2 3 |
|-----------------|---|--|-------------|
| | | ore | 4 |
| В. | Edema Formation Very slight edema (barely percepts Slight edema (edges of area well of Moderate edema (area raised appr Severe edema (raised more than 1) | ible)defined by definite raising) | 1 2 3 |
| | | e | 4 |
| | Total possible score for pr | rimary irritation | 8 8 |
| | | | |
| 2 or 1 2 - 5 | essmild irritantmederate irritant bovesevere irritant | Sensitization 2 or lessmild sensitiz 2 - 5moderate sen 6 or abovesevere sensi | sitizer |

SCORE SHEETS

Varisoft 222-90% Varisoft 110 Varonol SLES-60% Varonol SLES-30% Varonol SLS Varion 1017

Product Tested: Varisoft 222-90%

| | | | Erythema-eschar observation | | Edema observation | | | |
|---------|---------|-------|-----------------------------|--------|-------------------|--------|--------|---------|
| RABBIT# | SKIN | 4 hr. | 24 hr. | 48 hr. | 4 hr. | 24 hr. | 48 hr. | AVERAGE |
| 1 | Intact | 2 | 2 | 2 | 0 | 0. | 0 | 2.33 |
| | Abraded | , 2 | 2 | 2 | 0 | 1 | 1 | |
| 2 | Intact | 2 | 2 | 2 | 0 | 0 | 0 | 2.00 |
| | Abraded | 2 | 2 | 2 | 0 | 0 | 0 | |
| 3 | Intact | 2 | 2 | 2 | 0 | 0 | 0 | 2.50 |
| | Abraded | 2 | 2 | 2 | 1 | 1 | 1 | |
| 4 | Intact | 2 | 2 | 2 | 0 | 0 | 0 | 2.17 |
| | Abraded | 2 | 2 | 2 | 0 | 0 | 1 | |
| 5 | Intact | 2 | 2 | 2 | 0 | 0 | 0 | 2.00 |
| | Abraded | 2 | 2 | 2 | 0 | 0 | 0 | - |
| 6 | Intact | 2 | 2 | 2 | 0 | 0 | 0 | 2.00 |
| | Abraded | 2 | 2 | 2 | 0 | 0 | 0 | #* |

RATIO OF TISSUE DESTRUCTION:

| | Evaluation of | | o regarding six Observation tir | |
|-------------------|--------------------------------|------------|------------------------------------|------------|
| Test Site | Skin Reaction | 4 hrs. | 24 hrs. | 48 hrs. |
| Intact Abraded | Non-Corrosive Non-Corrosive | 6:6 6:6 | 6:6 6:6 | 6:6 6:6 |

Product Tested: Varisoft 110

| | | | ythema-eso observatior | | Ede | ma observa | ation | |
|---------|---------|----------|---------------------------|--------|-------|------------|--------|---------|
| RABBIT# | SKIN | 4 hr. | | 48 hr. | 4 hr. | 24 hr. | 48 hr. | AVERAGE |
| 1 | Intact | 2 | 2 | 2 | 0 | o | 0 | 2.00 |
| | Abraded | 2 | 2 | 2 | 0 | 0 | 0 | |
| 2 | Intact | 2 | 2 | 1 | 0 | 0 | 0 | 1.83 |
| | Abraded | 2 | 2 | 2 | 0 | 0 | 0 . | |
| 3 | Intact | 2 | 2 | 2 | 0 | 0 | 0 | 2.00 |
| | Abraded | 2 | 2 | 2 | 0 | 0 | 0 | |
| 4 | Intact | 2 | 2 | 2 | 0 | 0 | 0 | 2.00 |
| | Abraded | 2 | 2 | 2 | 0 | 0 | 0 | |
| 5 | Intact | 2 | 2 | 1 | 0 | 0 | 0 | 1.83 |
| | Abraded | 2 | 2 | 2 | 0 | 0 | 0 | - |
| 6 | intact | 2 | 2 | 1 | 0 | 0 | 0 | 1.83 |
| | Abraded | 2 | 2 | 2 | 0 | 0 | 0 | |

RATIO OF TISSUE DESTRUCTION:

| | Evaluation of | Ratio regarding six rabbits Observation time | | | |
|-----------|---------------|--|---------|---------|--|
| Test Site | Skin Reaction | 4 hrs. | 24 hrs. | 48 hrs. | |
| Intact | Non-Corrosive | 6:6 | 6:6 | 6:6 | |
| Abraded | Non-Corrosive | 6:6 | 6:6 | 6:6 | |

Federal Hazardous Substances Labeling Act

Varisoft 222-90% Varisoft 110 Varonol SLES-60% Varonol SLES-30% Varonol SLS Varion 1017

METHOD FOR PRIMARY IRRITATION-RABBIT SKIN FEDERAL HAZARDOUS SUBSTANCES LABELING ACT

The intact and abraded skin of 36 albino rabbits was used for this study. A series of 6 rabbits was used for testing each substance. The hair was clipped from the backs with the aid of angora clippers. Two areas of the back, placed approximately ten centimeters apart, were designated for the positions of the patches. One area was abraded by making four epidermal incisions (two perpendicular to two others in the area of the patch.) The patches consisted of two layers of light gauze cut in squares (2.5 cm. on the side). The patches were secured to the area by thin bands of adhesive tape. The material to be tested (0.5 ml.) was introduced beneath the patch. The entire trunks of the animals were then wrapped in clear plastic trunk bands. The trunk bands help to hold the patches in position and retards evaporation of volatile substances during the twenty-four hour exposure. The compound under test was applied so that there were two applications (one intact and one abraded) to each of six animals. The animals were immobilized in a special holder during the twenty-four exposure period. Upon removal of the patches the resulting reactions were evaluated on the basis weighted scores. Evaluations were again made after seventy-two hours. The final score represents an average of the twenty-four and seventy-two hour readings.

METHOD OF POINT SCORING

FOR

EVALUATION OF SKIN REACTIONS

| Α. | Erythema and Eschar Formation . | |
|----|---|----|
| | Very slight erythema (barely perceptible) | 1 |
| | Well defined erythema | 2 |
| | Moderate to sévere erythema | 3 |
| | Severe erythema (beet redness) to slight eschar formation | |
| | (injuries in depth) | 4 |
| | Total possible erythema score | 4 |
| В. | Edema Formation | |
| | Very slight edema (barely perceptible) | 1 |
| | Slight edema (edges of area well defined by definite raising) | 2 |
| | Moderate edema (area raised approximately 1 mm.) | 3 |
| | Severe edema (raised more than 1 mm. and extending beyond | |
| | area of exposure) | 4 |
| | Total possible edema score | 4 |
| | Total possible score for primary irritation | 78 |
| | or sensitization | 8 |
| | | |

Primary Irritation Index Sensitization

| 2 or lessmild irritant | 2 or lessmild sensitizer |
|---------------------------|------------------------------|
| 2 - 5moderate irritant | 2 - 5moderate sensitizer |
| 6 or abovesevere irritant | 6 or above severe sensitizer |

SCORE SHEETS

Varisoft 222-90% Varisoft 110 Varonol SLES-60% Varonol SLES-30% Varonol SLS Varion 1017

Product Tested

Varisoft 222-90%

Test Method

Draize Woodard and Calvery

| 7 NT: | IMAL | | | | | | |
|-------|-------|---------|---------|---------|---------|---------|--|
| MIN. | IWAL | INTACT | | ABI | ABRADED | | |
| NO. | SEX | 24 HRS. | 72 HRS. | 24 HRS. | 72 HRS. | AVERAGE | |
| 1 | М | 2/0 | 1/0 | 2/1 | 2/0 | | |
| 2 | F | 2/0 | 2/0 | 2/0 | 2/0 | | |
| 3 | F | 2/0 | 2/0 | 2/1 | 2/1 | 2.08 | |
| 4 | M | 2/0 | 2/0 | 2/0 | 2/1 | | |
| 5 | М | 2/0 | 1/0 | 2/0 | 2/0 | | |
| 6 | F | 2/0 | 2/0 | 2/0 | 2/0 | * | |
| | | | | | | | |
| | | | | | | | |
| | | - | | | | | |
| | | | | | | | |
| AVE | ERAGE | 1 | .83 | 2 | .33 | | |

Primary Irritation Index of Compound

2.08

Erythema/Edema

Product Tested

Varisoft 110

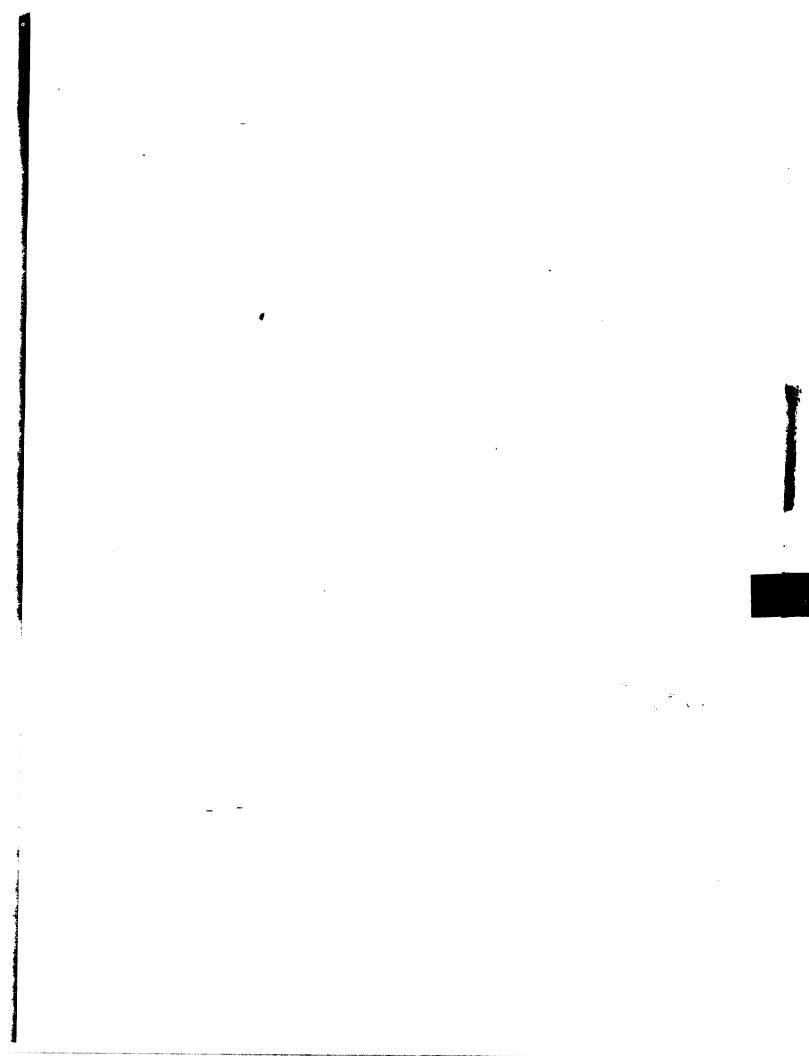
Test Method

Draize Woodard and Calvery

| ANIMAL | | | | | | |
|--------|-------|---------|---------|---------|---------------------|------|
| | | INI | ACT | ABI | COMBINED AVERAGE | |
| NO. | SEX | 24 HRS. | 72 HRS. | 24 HRS. | 72 HRS. | |
| 1 | М | 2/0 | 2/0 | 2/0 | 2/0 | |
| 2 | F | 2/0 | 1/0 | 2/0 | 2/0 | |
| 3 | F | 2/0 | 2/0 | 2/0 | 2/0 | 1.83 |
| 4 | M | 2/0 | 1/0 | 2/0 | 2/0 | • |
| 5 | M | 2/0 | 1/0 | 2/0 | 2/0 | à: |
| 6 | F | 2/0 | 1/0 | 2/0 | 2/0 | |
| | | | | | | |
| | | | | | | |
| | | | | | | |
| AVI | ERAGE | 1 | .67 | | .00 | |

Primary Irritation Index of Compound

Erythema/Edema



Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

Attachment 18:

Report to Ashland Chemical Company - Skin Sensitization Test with Varisoft 222 in Albino Guinea Pigs [PEQ 68410-69-5]

1

Industrial BIO-TEST Laboratories, Inc.

1810 FRONTAGE ROAD NORTHBROOK, ILLINOIS 60062

REPORT TO

ASHLAND CHEMICAL COMPANY

SKIN SENSITIZATION TEST WITH VARISOFT 222 IN ALBINO GUINEA PIGS

APRIL 10, 1973

IBT NO. 601-02910

Industrial BIO-TEST Laboratories, Inc. 1810 FRONTAGE ROAD

NORTHBROOK, ILLINOIS 60062

April 10, 1973

Mr. Robert B. McConnell Ashland Chemical Company Division of Ashland Oil, Inc. Chemical Products Division 2001 Afton Road Janesville, Wisconsin 53545

Dear Mr. McConnell:

Re: IBT No. 601-02910 - Skin Sensitization Test with VARISOFT 222 in Albino Guinea Pigs

We are submitting herewith our laboratory report dated

April 10, 1973, prepared in connection with the above study.

Very truly yours,

J. C. Calandra

President

JCC: sjn

REPORT TO

ASHLAND CHEMICAL COMPANY

SKIN SENSITIZATION TEST WITH

VARISOFT 222

IN ALBINO GUINEA PIGS

APRIL 10, 1973

IBT NO. 601-02910

I. Introduction

At the request of Ashland Chemical Company, a skin sensitization test was conducted with a sample identified as VARISOFT 222 (4% Solids Dispersion), Lot No. 152-12.

II. Summary

The results of the skin sensitization test in albino guinea pigs indicate that VARISOFT 222, Lot No. 152-12, is not a sensitizer.

Respectfully submitted,

INDUSTRIAL BIO-TEST LABORATORIES, INC.

Report prepared by:

Box + cley Knother as

Technician
Acute Toxicity

Report approved by:

Carmen Mastri, B.S. Senior Group Leader

Acute Toxicity

M. L. Keplinger, Ph. D.

Manager, Toxicology

chm

III. Investigational Procedure

Ten albino guinea pigs were used to evaluate the skin sensitizing properties of the test material. The test procedure employed was modeled after that of E. V. Buehler*.

Prior to the test, the irritation threshold of the test material in the appropriate vehicle was established. The hair was then clipped from the backs and flanks of the test animals, and each guinea pig was insulted every other day with a single closed patch containing a non-irritating concentration of the test material for a total of nine insults.

Closed patches were applied to the guinea pigs in the following manner:

A Webril pad containing 0.5 ml of a 1.0% (w/v) aqueous solution of the test material was applied near the midline of the shaved back of each animal. The Webril pad was occluded with a standard size Elastoplast coverlet (1-1/2 inch x 2 inches) and each animal was placed in a guinea pig restrainer for a six-hour exposure period. The application sites were scored for irritation 24 and 48 hours after the initial insult and 24 hours after each of the remaining eight insults.

Two weeks after the last insult, all test animals and four control animals from the same population were challenged with duplicate patches. The application sites on each animal were scored for irritation 24 and 48 hours after challenge. Any reaction noted among the test animals at challenge that was greater than that noted among the control animals was considered evidence of sensitization.

The scoring criteria for erythema and edema are presented in Table I.

Duehler, E.V., "Delayed Contact Hypersensitivity in the Guinea Pig,"

Arch. Dermat. 91, February 1965.

TABLE I

Skin Sensitization Test - Albino Guinea Pigs

Scoring Criteria for Skin Reactions

| Reaction | Description | Score |
|-----------------|---|-------|
| Erythema | Barely perceptible (Edges of area not defined) | 1 |
| • | Pale red in color and area definable | 2 |
| | Definite red in color and area well defined | 3 |
| | Beet or crimson red in color | 4 |
| Edema | Barely perceptible (Edges of area not defined) | 1 |
| | Area definable but not raised more than 1 mm | 2 |
| | Area well defined and raised approximately 1 mm | 3 |
| | Area raised more than 1 mm | 4 |
| Injury in Depth | Escharosis, Necrosis | 8. |
| | Maximum Primary Skin Irritation Score | = 8 |

IV. Results

The results of the skin sensitization test are presented in Tables
_H - IV.

TABLE IV

TEST MATERIAL: 1.0% (w/v) Aqueous Solution of VARISOFT 222

Skin Sensitization Test - Albino Guinea Pigs

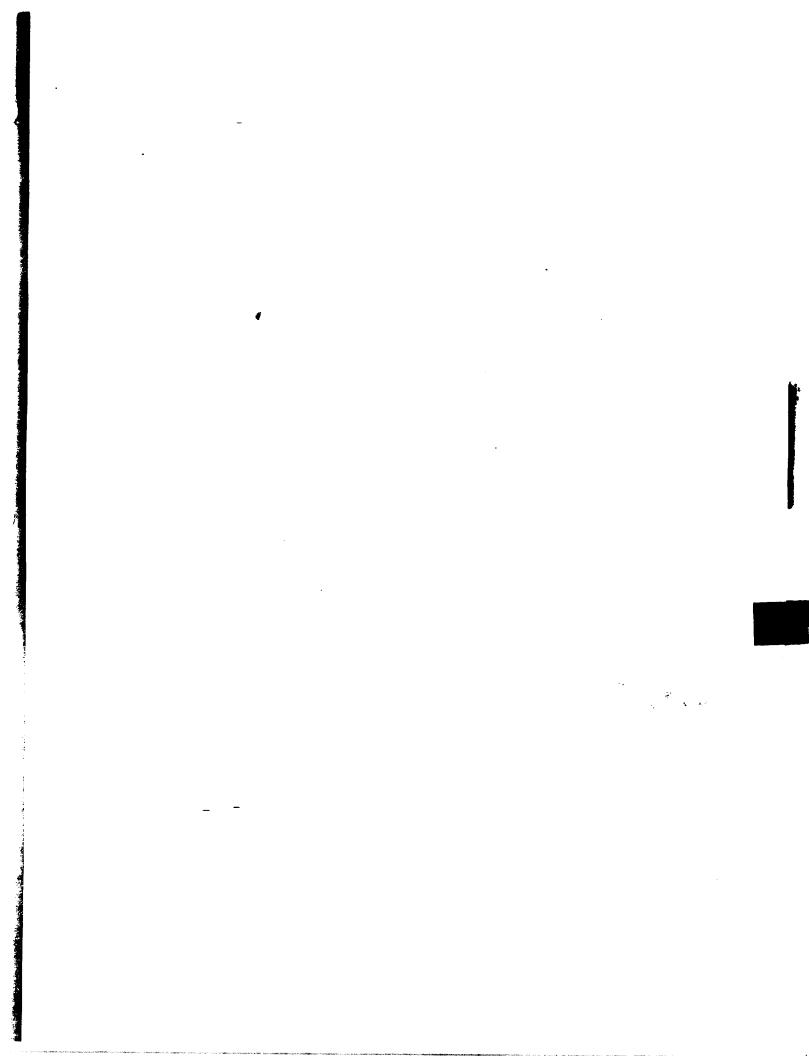
Results - Control Group

| | Scores Following Challenge Applications Site 1 Site 2 | | | | | | | |
|--------|---|-----|----------|-----|----------|-----|----------|----|
| Animal | 24 Hours | | 48 Hours | | 24 Hours | | 48 Hours | |
| Number | Er. | Ed. | Er. | Ed. | Er. | Ed. | Er. | Ed |
| 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| · 3 | 0 | 0 | 0 | . 0 | 0 | 0 | 0 | 0 |
| 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0. |

Key:

Er. = Erythema

Ed. = Edema



Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

Attachment 19:

Delayed Contact Hypersensitivity Study in Guinea Pigs [PEQ 68410-69-5]

SPRINGBORN INSTITUTE FOR BIORESEARCH.INC.

SPENCERVILLE, OHIO 45887

PHONE 419 647-4196

DELAYED CONTACT HYPERSENSITIVITY STUDY IN GUINEA PIGS

Varisoft 222-90

Sample: Lot V2010225

Lab Study No.: 3063.12 Report Date: 1/18/82

Protocol: Delayed Contact Hypersensitivity

Sponsor: Sherex Company

5200 Blazer Parkway Dublin, OH 43017

| Enclosed: | Page |
|--------------------------|-------|
| Summary | 2 |
| GLP Requirements | 3 |
| | 4 |
| Raw Data Appendix | 5-10 |
| | 11-18 |
| Pertinent Communications | |
| Protocol Amendment | None |

Signed:

Richard A. Hiles, Ph.D. Vice President and Director of Acute and Subchronic Toxicology

(Study Director)

Jon C. Fulfs, Ph.D President and Director of Toxicology

Addendum to Final Report

DELAYED CONTACT HYPERSENSITIVITY--SUMMARY

Report of a biological test performed at:

Springborn Institute for Bioresearch, Inc. 553 North Broadway Spencerville, Ohio 45887

During the period: 11/2/81 to 1/18/82 According to the attached protocol and addenda (if any). Deviations from Protocol: None

* * *

Lab Study No.:

3063.12

Sponsor's Reference:

Letter of October 26, 1981

Test Substance (TSIN):

Varisoft 222-90 Lot V2010225

Description:

Pinkish dull paste

Storage Conditions:

Ambient

Sponsor's Divisional Toxicologist: Robert L. Harrison

Strain and Source of Animals:

Hartley Albino Guinea Pigs

Isaacs Lab Stock

Concentration and Amount of Test Substance Dosed:

Induction: 25% Varisoft 222-90 in 80% Ethano Challenge: 2.5% Varisoft w/v in Acetone

Rechallenge: 2.5% Varisoft w/v in distilled H2

5.0% Quat A w/v in 95% ETOH

0.5% 1208-0S w/v in 95% ETOH²

| | | RI | ESUL TS | 7 | | | | |
|--------------------|---------|-------|----------------|-------|-------|------------------|-------|--|
| | ĺ | | | Seve | rity | Max. Score | | |
| Treatment | t e | Level | Incidence | 24 hr | 48 hr | 24 hr | 48 hr | |
| Primary Challenge: | Test | 2.5% | 18/19 | 1.1 | 0.7 | 2 | 1 | |
| (Varisoft) | Control | 2.5% | 0/10 | 0.0 | 0.1 | 0 | ± | |
| Rechallenge: | Test | 2.5% | 0/19 | 0.1 | 0.1 | * (± , . | ± | |
| (Varisoft) | Control | 2.5% | 0/6 | 0.0 | 0.0 | Ō | 0 | |
| (Quat A) | Test | 5. | 15/19 | 1.0 | 0.6 | 2 | 1 | |
| (200) | Control | 5% | 1/6 | 0.5 | 0.3 | 1 | 1 | |
| (1208-OS) | Test | 0.5% | 13/19 | 0.9 | 0.6 | 2 | 1 | |
| (1200 00) | Control | 0.5% | 0/6 | 0.1 | 0.1 | ± | ± | |
| | | | | | | | | |
| | ļ | | | : | | | | |

Conclusions: See page 2(A).

From study 3063.11.

²From studies 3063.8, 3063.9, 3063.10.

CONCLUSIONS

Eighteen of nineteen guinea pigs challenged with 2.5% Varisoft 222-90 in acetone exhibited positive (> 1 score) responses following three induction exposures with a 25% preparation of Varisoft in ethanol. (The induction exposures caused moderate irritation.) All test animals were rechallenged with 2.5% Varisoft in water and no (0 of 19) animals exhibited positive responses. Thus, the acetone enhances the response to Varisoft probably by changing the absorption of the test article. The test animals were also exposed to 5% Quat A in ethanol and 0.5% 1208-0S in ethanol at the rechallenge with 15 of 19 and 13 of 19 positive responders, respectively. Thus, under certain defined conditions, Varisoft can elicit a sensitization response with cross reactivity to Quat A and 1208-0S. There are conditions under which Varisoft does not elicit a sensitization response.

GLP REPORT REQUIREMENTS

| GLP Requirement | |
|--|------|
| Name and Address of Test English | Page |
| Name and Address of Test Facility | 2 |
| Date Study Initiated | 2 |
| Date Study Completed | 2 |
| Objective and Procedures | |
| Statistical Methods Used | 11 |
| | NA |
| Test and Control Article Identification | 12 |
| Stability of Test and Control Articles | NA |
| Description of Methods | 12 |
| Description of Test System | _ |
| Species, Strain, Substrain, Source of Supply, Age, Sex, Body Weight Range, Number of Animals Used, and Procedure Used for Identification | 12 |
| Dosage Information | 13 |
| Description of Circumstances Which May Have Affected the Data | NA |
| Name of the Study Director | |
| Names of Other Scientist | 1 |
| Names of Other Scientists, Professional, and Personnel Involved in this Study | 1 |
| Description of Operations Performed on the Data | |
| A Summary and Analysis of the Data | 15 |
| A Statement of Conclusions Decree | 2 |
| A Statement of Conclusions Drawn from the Analysis | 2 |
| Signed and Dated Reports of Individual Scientists or Other Professionals Involved in the Study | 1 |
| Locations Where All Specimens, Raw Data, and Final Report are to be Stored | 4 |
| Quality Assurance Statement (signed) | |
| to to to to to to to to to to to to to t | 4 |

NA = Not Applicable

QUALITY ASSURANCE STATEMENT

| Study No | 3063.12 | Test | Substance | Varisoft 222-90 Lot V2010225 |
|--|------------|-------------------------------|----------------------------|-----------------------------------|
| Type of Study | Delayed (| Contact Hypers | ensitivity | |
| Listed below a Assurance Unit Director and t | CIIC GGC | ca illuninge we | was inspect ere reporte | ed by the Qualityed to the Study |
| Dates of Inspection | Dates Fine | dings Reported dy Director | | Findings Reported o Management |
| 1-12-82 1-15-82 | | 18-82 18-82 | | 1-18-82 1-18-82 |
| | | | | |

Location of Raw Data Storage Statement

The original copy of the final report and all raw data will be on file at the testing facility.

Carol S. Davis

Date 1-18-82

Director

Quality Assurance Unit

PRIMARY IRRITATION OBSERVATIONS -- SCREEN

Study No. 3063.12 Test Article Varisoft 222-90

| | Animal | | | Expo: Leve 25% | el | Le ¹ | osure vel 5% | **** | ≘1 0% | Expos Leve | el (|
|---|----------------|-----------|-----|----------------------|--------|-----------------|--------------------|-------|----------|---------------|----------|
| l | G- | -81 | Sex | 24 hr | 48 hr | 24 hr | 48 hr | 24 hr | 48 hr | 24 hr | 48 hr |
| 1 | "- 998 | _ " | F | 2 | 1 | 1 | ± | 1 | 1 | 1 | ± |
| 2 | "- 999 | _ " | Ŧ | 2 | 1 | 1 | ± | 1 | <u>+</u> | ± | 0 |
| 3 | "- 1000 |) - " | F | 2 | 2 | 1 | 1 | 1 | 1 | ± | ± |
| 4 | <u>"- 1001</u> | <u>-"</u> | F | . 2 | 1 | 2 | ± | 2 | 1 | ± | <u>+</u> |
| 5 | *_ | | | | | | | | | | |
| 6 | "_ | -" | | | | | | | | | |

Test Article Level: 25% 15% 10% 5₿ Incidence: 4/4 4/4 Severity: Sum (24 hr/48 hr) 8.0 /5.0 Avg (24 hr/48 hr) 2.0 /1.3 5.0 / 2.5 5.0 / 3.5 2.5 /1.5 /1.3 1.3/ 0.6 0.6 /0.4

| | Animal No | o. Bl Sex | Expos Leve 2.5 24 hr | | Lev | sure vel 0% | Expos Leve 0. 24 hr | el | Expos Leve | 1 |
|---|------------------|--------------|-------------------------------|---|-----|-------------------|------------------------------|----|---------------|---|
| 1 | "- 1032-" | | ± | ± | 0 | 0 | 0 | Ó | a 0 | 0 |
| 2 | "- 1033-" | М | <u>+</u> | ± | 0 | 0 | 0 | 0 | , 0 | 0 |
| 3 | "- 1034-" | F | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 4 | <u>"- 1035-"</u> | F | <u>+</u> | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 5 | HH | | | | | | | | | |
| 6 | " " | . - | | | | | | | | |

| Test Article Level: Incidence: | 2.5% | 1.0% | 0.5% | 0.25% |
|--------------------------------|---------|---------|-----------|-----------|
| Severity: | | | | |
| Sum (24 hr/48 hr) | 1.5/1.0 | 0.0/0.0 | 0.0 / 0.0 | 00/00 |
| Avg (24 hr/48 hr) | 0.4/0.3 | 0.0/0.0 | 0 0 / 0 0 | 0.0 / 0.0 |

PRIMARY IRRITATION OBSERVATIONS -- SCREEN

| St | udy No. | 306 | 3.1 | 2 | · · · · · · · · · · · · · · · · · · · | Test Ar | ticle | Varis | oft 22 | 2-90 | |
|--------------|---|--------------|------------|---------------|---------------------------------------|--------------|--------------|---------------|-------------|---------------|-------------|
| | | | | | | | | | | | |
| | Animal | | | Lev 2 | . 5 % | Le 1 | osure vel | Lev | sure vel | Expo | sure 'el |
| | | -81 | | | 48 hr | 24 hr | 48 hr | 24 hr | 48 hr | 24 hr | 48 h |
| | | | M | 1 | nd Dead | | | <u> </u> | | | |
| | | | M | 0 | 0 | 0 | 0 | ļ | | | |
| | | | F | 0 | 0 | 0 | 0 | | | | |
| | 1 "- 1057 | | F | 0 | 0 | 0 | 0 | <u> </u> | | | |
| | 5 "- | | | | | | | | | | |
| |) "- | _ " | | <u> </u> | | | | | | | |
| Sev Su | cidence: verity: um (24 hr vg (24 hr | ·/48 ·/48 | hr) hr) | 0.0 | / 0.0 | 0.0 / | ′0.0 | | / | | / |
| | Animal | No. | | Expos Leve | 1 | Expo Lev | sure el | Expos Leve | | Expos Leve | |
| | i | | Sex | 24 hr | 48 hr | 24 hr | 48 hr | 24 hr | 48 hr | 24 hr | 48 hr |
| 2 | | -"- | | | | | | | | à. | |
| 3 | | -" | | | | | | | | | |
| 4 | | -"- | | | \longrightarrow | | | | | | |
| 5 | | -" | | | | | | | | | |
| 6 | | | | | | | | | | | |
| Test Inci | Article | Lev | /el: | | | | | | | | |
| Sum | rity: a (24 hr/ a (24 hr/ | 48 h | r) (r) | | | | | | | | |

(7)
OBSERVATIONS--TEST

| | | 2242 12 | | | Varisoft | | |
|-------|-----|---------|------|---------|-----------------|-------|-----------|
| Study | No. | 3063.12 | Test | Article | 222-90 | Phase | Challenge |
| | | | | - | | | CHATTCHE |

Last induction 12/3/81, Challenge 12/16/81

| | 1 | | | T | Fync | sure | N 5 | | | | | |
|------|---------------|------|------|------|-------|------------|-------|------------|-------|-------------|--|--|
| | | | ŗ | | Leve | | Expo | osure | Expos | | | sure |
| | Anim | mal | No. | 1 ' | | 5 % | / re, | vel | Leve | eT. | Lev | el |
| | G- | | -81 | Sex | 24 hr | 48 hr | 24 pr | 48 hr | 24 hr | 48 hr | 24 hr | 148 hr |
| 1 | L "- 9 | 974 | _# | М | | ± | | | | | | 1 |
| 2 | | 975 | _ " | М | 1 | ± | | \ | | | | |
| 3 | , - ! | 976 | _ = | М | 1 | ±* | İ | | | | | |
| 4 | 9 | 977 | _ " | М | 1 | 1 | | | | | i | |
| 5 | - 9 | 978 | _" | М | 1 | 1 | | | | | | |
| 6 | | | | М | 1 | ±* | | | | | | |
| 7 | m_ 9 | 980 | _ # | М | 1 | ± | | | | | | |
| 8 | - 9 | 381 | _# | М | 1 | ±* | | | | | | |
| 9 | . 9 | 982 | _ " | М | De | ad | | | 1 A | | | |
| 10 | * _ 9 | 183 | _ " | М | 1 | 1* | | | | | | |
| 11 | - 9 | 184 | _ " | F | 2 | 1* | | | | | - | |
| 12 | | | | F | 1 | ±* | , | | | | | |
| 13 | | | | P | 2 | 1* | | , <u> </u> | | <u> </u> | | |
| 14 | - 9 | | | F | 0 | 0* | , | , j | | ÷ | | |
| 15 | | | | F | 1 | ±* | | | | 1 | | <u> </u> |
| 16 | - 9 | | | F | 1 | ± | | | | | , \ <u>\</u> | 1 |
| 17 | " _ 9 | | | F | 1 | 1 | | | | | , | |
| | "_ 9 | | | F | 1 | ± | | | | | | \ |
| | " _ 99 | | | F | 1 | ±* | | | | | • | |
| 20 | "_ 99 | 93 . | _" | F | 1 | 1 | | | | | | |
| rest | : Art | icle | e Le | vel: | 2.5 | · • | | <u> </u> | | <u>P</u> | <u></u> | |
| ٠ و | | | | | | <u> </u> | | | | | | |

| Test Article | Level: 2.5% | • | |
|--------------|-------------|---|--|
| Incidence: | 18/19 | | |
| Severity: | | | |

Sum (24 hr/48 hr) 20.0/12.5 / / / / / / Avg (24 hr/48 hr) 1.1/ 0.7

^{*}See page (7A).

During the grading at 24 nours, I noticed that around the test site there seemed to be an interaction between the tape of the patch and the skin. This was in some control and some test animals. This skin was a little redder than the patch area particularly in the controls. The technician noted that the tape had stuck rather firmly to some animals. We did not systematically record this observation at the 24 hour reading.

At the 48 hour reading, we noted the involved animals with an asterick. In the test animals the tape area was often redder than the test site by one grade. However, in the control and in the test animals more often than not the hair had not grown back in the involved tape area. There was no sign of irritation in the tape area of the involved control animal but rather no hair growth.

OBSERVATIONS -- CONTROL

| St | udy | No3 | 063. | 12 7 | Cest Ar | ticle_ | Varisof 222-90 | | nase_Ch | alleng | e |
|--------------------|------------|--------------------------|------------|-------|------------------------------|--------|-------------------|-------|-------------------|-------------------|--------------|
| | Cha | llenge l | 2/16/ | '81 | | | . • | | | | |
| | An G- | imal No. | | Lev | Exposure Level 2.5% Arj48 hr | | Exposure Level | | Exposure Level | | sure |
| 1 | " _ | 1079-" | M | _ | 48 NF | 24 hr | 48 hr | 24 hr | 48 hr | 24 hr | 48 hr |
| 2 | T | 1080-" | м | | ± | | | | | | |
| 3 | | 1081-" | М | 0 | 0* | | | | | | |
| 4 | " _ | 1082-" | М | 0 | 0* | | | | | | |
| 5 | * - | 1083-" | М | 0 | 0* | | | | | | |
| 6 | " - | 1084-" | F | 0 | 0 | | | | | | - |
| 7 | - | 1085-" | F | 0 | 0* | | | | \longrightarrow | | |
| 8 | "- | 1086-" | F | 0 | 0* | | | | | $\overline{}$ | |
| 9 | "- | 1087-" | F | 0. | 0* | | | | | \longrightarrow | |
| 10 | <u>"-</u> | 1088_# | F | 0 | 0* | | | | | <i>-</i> | |
| rest | : Ar | ticle Le | vel: | 2. | 5% | | | | | | 1 |
| Inci | den | ce: | | | 10 | | | | <u></u> | | |
| Seve Sum Avg | (2 | y: 4 hr/48 4 hr/48 | hr) hr) | 0.0 / | 0.5 | / | | / | | | |
| *Se∈ | pa | g e (7A). | | | | | | | | | |

OBSERVATIONS--TEST

Study No. 3063.12 Test Article Quat A Phase Rechallenge 1208-08

| | An G- | imal | | <i>*</i> | Leve 2.5% | Vari ₊ | Lev 5% Qua | | | el L208-0s | | Čev | |
|----|-----------|------|-----|----------|--------------|-------------------|---------------|-------|----------|---------------|---------------------------------------|-------------|--------------|
| | + | 074 | | | | 48 hr | | 48 hr | 24 hr | 48 hr | 24 | hr | 48 hr |
| _1 | + | 974 | | M | | 0 | 1 | ± | ± | ± | | | |
| 2 | <u>"-</u> | | | М | 0 | 0 | ± | ± | 1 | ± | | | |
| 3 | "- | 976 | _" | М | 0 | 0 | 1 | , ± | 1 | ± | 1 | | |
| 4 | "- | 977 | _" | М | ± | 0 | 1 | ± | 1 | ± | | \ | |
| 5 | "- | 978 | _" | М | 0 | 0 | 2 | 1 | 2 | 1 | | | |
| 6 | "- | 979 | _" | М | 0 | 0 | 1 | ± | ± | <u>+</u> | | 1 | |
| 7 | "- | 980 | _" | М | ± | 0 | ± | ± | ± | ± | | \forall | |
| 8 | "_ | 981 | _" | М | 0 | 0 | 1 | 1 | 1 | ± | | $- \forall$ | |
| 9 | " _ | 982 | _" | М | Dea | đ | | | | | · · · · · · · · · · · · · · · · · · · | | |
| 10 | "- | 983 | _" | М | 0 | . 0 | ī | 1 | 1 | 1 | | \dashv | |
| 11 | "_ | 984 | _ " | F | 0 | 0 | 1 | ± | 1 | | | | + |
| 12 | "- | 985 | _ " | F | 0 | 0 | 1 | ± | 1 | ± | | | + |
| 13 | "_ | 986 | _ " | F | 0 | 0 | 1 | ± | 1 | ± | | - | |
| 14 | "_ | 987 | _" | F | 0 | ± | 1 | ± | 1 | ± # | ÷' | | + |
| 15 | "_ | 988 | _ " | F | 0 | 0 | 1 | 1 | 1 | 1 | 4 5 | • | -+ |
| 16 | "_ | 989 | _" | F | 0 | 0 | 1 | ± | ± | ± | | _ | |
| 17 | "- | 990 | _ " | F | 0 | 0 | ± | ± | <u> </u> | ± | | \dashv | |
| 18 | "_ | 991 | _ " | F | 0 | 0 | 2 | 1 | 2 | 1 | | | -+ |
| 19 | "_ | 992 | ."_ | _ F | 0 | 0 | 1 | ± | <u> </u> | ± | | - | + |
| 20 | "_ | 993 | ." | F | 0 | 0 | 0 | 0 | 1 | 1 | | \dashv | |

| 20 | | | _ + | + | | Ì |
|---|-------------------------|-----------------------|-------|----------------|---|---|
| Test Article Level: Incidence: | 2.5% Vari- 0/19 SOFE | 5% Quat A 15/19 | 0.5% | 1208-0 3/19 | S | |
| Severity: Sum (24 hr/48 hr) Avg (24 hr/48 hr) | | 18.5/11.5 1.0/ 0.6 | 18.0/ | 12.0 | / | , |

(10)

OBSERVATIONS -- CONTROL

Varisoft
Quat A
Study No. 3063.12 Test Article 1208-05 Phase Rechallenge

| | 1 | | i . | Expo: | | Expo | sure | Exposure \ Exposure | | | | |
|----------|------------|----------|-----|--------------|--------------------------------|------|---------------|----------------------|--------|-------------------|--------------|--|
| 1 | Ani | imal No. | | Leve 2.5% | Level 2.5% Variate 24 hr 48 hr | | vel Quat A | Level 0.5% 1208-0 | | Exposure Level | | |
| <u> </u> | G- | -81 | | 24 hr | 148 hr | | 48 hr | 24 hr | 1208-0 | | 140 | |
| 1 | | 1109-* | M | 0 | 0 | ± | 0 | 0 | | 24 hr | 48 hz | |
| 2 | | 1110-" | M | 0 | 0 | ± | ± | | 0 | | | |
| 3 | *_ | 1111 | М | 0 | 0 | | | 0 | 0 | | | |
| 4 | w_ | 1112-" | F | 0 | | ± | 0 | 0 | 0 | | | |
| 5 | | 1113-" | | | 0 | ± | ± | 0 | 0 | | \ | |
| | | | F | 0 | 0 | 1 | 1 | ± | ± | | | |
| 6 | | 1114-" | F | 0 | 0 | 0 | 0 | 0 | 0 | | | |
| 1-4 | #= | | | | | | | | | | \ | |
| 8 | " - | _ " | | | | | | | | | - | |
| 9 | "- | _" | | · | Ĭ | | | | | | | |
| 10 | " _ | _ " | | | <u>_</u> | | | | | | | |
| | | | | 2 50 | <u>_</u> | | J | | | | | |

| Test Article Level: Incidence: | 2.5% Vari- soft 0/6 | 5% Quat A | 0.5% 1208-0S 0/6 | |
|---|---------------------------|------------------------|---------------------|--|
| Severity: Sum (24 hr/48 hr) (24 hr/48 hr) (24 hr/48 hr) | 0.0 / 0.0 | 3.0 / 2.0 0.5 / 0.3 | 0.5 / 0.5 | |

SHAMOROWN MR HATTE I ON MICHIEF BILL

DELAYED CONTACT HYPERSENSITIVITY (Buehler Method - Modified)

3063.12

PURPOSE

To determine if a test article elicits a delayed contact hypersensitivity response in guinea pigs so that it may be compared with more familiar substances.

TEST ARTICLE

| All test articles are furnished by the sponsor. They are identified as follows: | |
|--|------------|
| Varisoft 222-90 Lot V2010225 \$81.0/9.3063 | |
| The sponsor assumes responsibility for any necessary evaluations for purity, strength, stability, etc. | |
| Storage Conditions: <u>Ambient</u> | |
| Known Hazards: Eye irritant, mildly irritating to the skin | L |
| Sherex Company 5200 Blazer Pkwy Dublin, Ohio 43017 TESTING FACILITY | |
| Springborn Institute for Bioresearch, Inc. Spencerville, Ohio 45887 (419) 647-4196 | . , |
| PROPOSED STARTING DATE | |
| ///2/4/ (completed by SIB) PROPOSED COMPLETION DATE | |
| (12 weeks from receipt of test article) | |

LTTERS A REPORTS. Springborn Institute for Biotic worch, Inc. and Springborn Group, Inc. letters and reports are issued for the exclusive use for the cities to whom they are addressed. No quotations from reports or use of the Springborn Institute for Bioresearch, Inc. and Springborn in products or survived except as expressly authorized in writing. Letters and reports apply only to the specific materials products or cities and in the labelity of Springborn Institute for Bioresearch, Inc. and Springborn Group, Inc. with respect to service materials, products and to the amount of consideration poid for such services and not in the any consequential damages.

Study No. 3063.12

(12)

TEST SYSTEM JUSTIFICATION

The guinea pig is the classical animal for determining delayed contact hypersensitization.

ANIMALS

Albino Guinea Pigs, Isaacs Lab Stock. Equal numbers of males and females is desirable.

20 animals - test animals

10 animals - negative control

4 animals - primary irritation evaluation,
• if required

Acclimated ≥ 4 days and treat for 4 days during this period for internal parasites. Animals are of a size to fit the restrainers.

ANIMAL IDENTIFICATION

For scientific reasons, individual animals are not identified by ear tag, toe clip, etc. Each cage and restrainer is marked with the animal number. Careful attention is given to see that the proper animal goes into the proper restrainer during treatment and is returned to the proper cage.

HOUSING AND ANIMAL CARE

One/cage during testing in elevated wire mesh cages. 12/12 hour light/dark cycle. Other items according to AAALAC standards.

FOOD AND WATER

Commercial laboratory feed and water freely available at all times.

ADMINISTRATION OF TEST ARTICLE

Irritation Screen:

Exposure of the guinea pigs can be divided into three phases: Irritation, Induction and Challenge.

The Irritation phase has the purpose of determining the proper level of test article to use in the Challenge phase. This proper level should be the highest level which will not cause irritation when applied to the guinea pigs under the conditions which will be used in the Challenge phase. If the test article is known not to be an irritant, the irritation evaluation need not be run. If the irritation potentials are unknown, four levels of test article are normally evaluated using the same

BANKER BELLING BELLITUIE FOR HICHE AND AND ARCH PIC

solvent which will be used in the "Challenge Phase". If all tested levels cause irritation, additional levels may need to be run. Appendix B is a format for exposure; the position of the different concentrations should be varied to adjust for possible site-to-site variations. The irritation evaluation can be done before or during the induction phase.

Do not run an irritation evaluation.

Run an irritation evaluation at the following concentration or amounts using Acetone as a solvent:

25 90 W/V 2. 3.

To be established by Elvin Newmann (Procter & Gamble)

warm it needled

Remove the hair from the back using a small animal clipper. Do this the day before applying the test article. Apply closed patches to the animals in the following manner (one patch for each level of test article): Apply 0.4 ml of the freshly prepared test article on a 20 X 20 mm Webril pad on a 37 X 40 mm Parke-Davis Readi-Bandage. Put the animal in the restrainer and apply the patch(es) to the clipped surface as quickly as possible after the substance has been applied to the patch. Occlude the patch with a rubber dental dam pulled taut and fastened to the bottom of the restrainer with clips. Adjust the restrainer to minimize movement of the animal during exposure. Six (6) hours later (5 1/2-6 1/2 hr), remove the dental dam and patch(es), take the animal from the restrainer and place it in its cage.

Approximately 24 hours after initiating the irritation exposure, depilate all animals as described in the "Challenge Phase" and grade the test sites. BINDER CLIPS DAMPONS

NOTURED CHESTRAIN PS 1/1

SOLURED CHESTRAIN PS 1/1

Induction Phase:

The purpose of this phase is to dermally expose the animals to test article over a long enough period of time such that if the material is a sensitizer, the animal can develop an immunological response. The level of test article use may be irritation, though it is not necessary, but cannot be so high as to cause excessive systemic toxicity (i.e., death). A level several times greater than the anticipated human exposure should be used if possible. If a solvent other than water is used, it should be different than the solvent which will be used in the "challenge phase."

EThinol /14,0 - whom if needed

[ு]ம் கொளியிடுந்தும் நம்பும் de Bioresearch, Inc. and Springborn Group, Inc. letters and reports are issued for the exclusive use of the cients to whom they are addressed. No quotations from reports or use of the Springborn Institute for Bioresearch, inc. and Springborn Group, inc. name is permitted except as expressly authorized in writing. Letters and reports apply only to the specific materials, products or processes tested, examined or survivived and are not necessarily indicative of the qualities of apparently identical to smilar materials, products or triplinesses. The Labelland of Springborn love to the Residue of Springborn Group. 11 princesses. The Lability of Sprincipora Institute for Biorescarch in and Springuistin Group for with respect to services recifered shall be

00000 00000

clip the left shoulder of each animal with a small clipper the day before exposure. Apply closed patches to the animals in the test group(s) in the following manner: Apply 0.4 ml of the freshly prepared test substance or solution or a weighed amount of powder on a 20 X 20 mm Webril pad on a 37 X 40 mm Parke-Davis Readi-Bandage (Parke-Davis and Company, Greenwood, South Carolina). Put the animal in the resultand and apply the patch to the clipped surface as quickly as possible patch. Occlude 500 per// the patch with a rubber dental dam pulled taut and fastened to the bottom of the restrainer with binder clips. Adjust the restrainer to minimize movement of the animal during the exposure period. Six (6) hours later, remove the dental dam and patch, take the animal from the restrainer, and place it in its cage. Remove extremely viscous substances by a gentle rinse with warm water before returning the animals to their cages. the procedure at the same site once a week for the next two (2) weeks for a total of three 6-hour exposures (the interval between induction exposures may vary from 5 to 9 days). After the last induction exposure, leave the animals untreated for approximately two (2) weeks (12-16 days) before primary challenge.

Challenge Phase:

The test animals which have had three previous exposures to the test material are again exposed in the challenge phase. In addition, ten animals which have never been exposed to the test article are treated. The level of test article used is the one requested by the sponsor or the one determined in the irritation screen and should be a non-irritating dose. Some organic solvents can elicit a sensitivity response. If a solvent other than water has been used in the induction phase, a different solvent should be used in the challenge phase.

To be established by Elvin Newmann- Procter & Gamble [based on donlishin]
Test article concentration or level

| | | ~ - | |
|---------|----------|-----|--|
| | , | | |
| | / · | | |
| 0-3. | acetine | | |
| Solvent | AMUMM | | |
| | MULTUTUL | | |
| | | | |

Challenge the animals previously exposed during the induction period as well as the previously untreated control animals approximately two (2) weeks after the last induction exposure (the time between the last induction exposure and the challenge may vary from 12 to 16 days). Use the same patching procedure as for the "Induction Phase", but apply the patches to a skin site that has not been exposed previously (Appendix A). The site for challenge may be varied if necessary to achieve the objectives of the experiments (e.g., using multiple samples at challenge will require using several sites).

Approximately twenty-four (24) hours after initiating the primary challenge, depilate all animals with Neet Cream or Lotion Hair Remover (Whitehall Laboratories, Inc., New York). and leave it on for no more than thirty (30) minutes. Thoroughly wash off the depilatory with a stream of warm, to their cages.

A minimum of two (2) hour after depilation, grade the test sites on a scale of 0 to 3 (0 - no reaction, ± = slightly patchy erythema, 1 = slight, but confluent or moderate, with or without edema). Repeat the grading 24 hours later (48 hour grades).

Grades of 1 or greater in the test group indicate sensitization, provided grades of less than 1 are seen on control animals. If grades of 1 or greater are noted on control animals, then the reactions of test animals that exceed the most severe control reaction are presumed to be due to sensitization.

Rechallenge - The sponsor will be notified of animals that are considered sensitized. Verbal instructions for rechallenge will be given by the Sponsor, followed by written confirmation. Animals considered sensitized can be rechallenged 6-10 days after primary challenge, but not before.

REPORT

Report should include date the study was initiated and terminated and the results of both the challenge and any rechallenge in terms of incidence and severity of responses.

- (1) Incidence The number of animals in each group showing responses of 1 or greater at either 24 or 48 hours divided by the total number of animals tested in that group (e.g., 10/20).
- (2) Severity The sum of the test grades divided by the total number of animals tested in a given group determined for both 24 and 48 hours (e.g., 0.8 0.7). Grades of + are equal to 0.5 for calculation of severity indices. All average grades are to be rounded off to the nearest tenth of a unit.

Study No. 3063.12

00014

SHIRKHICHE PIGITUTE FOR BEINEAM ARCH MC

NOTICE

This study is run according to the principles of GLP's. If after a study is underway it becomes necessary to make changes in the approved protocol, the revisions and reasons for change are to be documented, reported to the Sponsor and are to become part of the permanent file for that study. Similarly, the Sponsor is to be notified as soon as is practical whenever an event occurs that is unexpected and may have an effect on the validity of the study.

1 to the

DATA RETENTION

The raw data and the original of the final report will be on file at the testing facility. The sponsor will be notified before final disposition of these items. test articles will be destroyed unless requested otherwise.

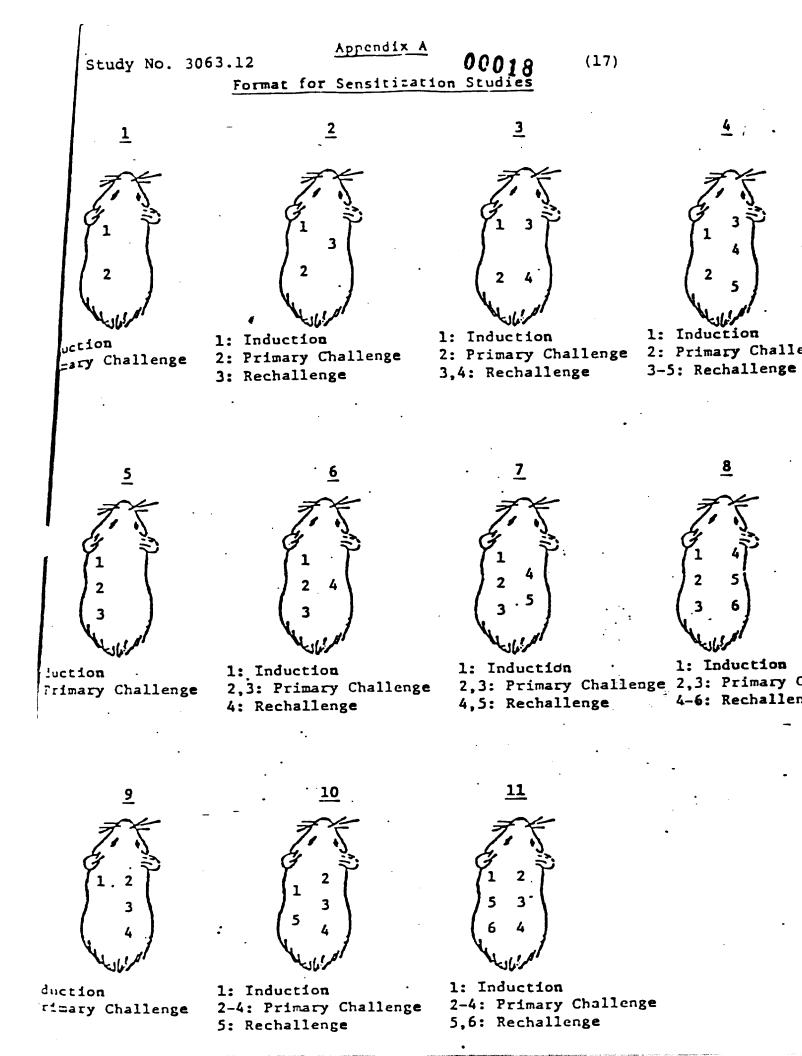
REGULATORY AGENCY

| (ager | cy_ | | | | _). | | | | |
|-------|------|------|------|----------|-----|----|------------|------|------|
| | _ | be | subn | $_{	t }$ | to | a | regulatory | agen | су |
| This | stud | ly ' | will | probably | not | be | submitted | Χ, | will |

Richard A. Hiles, Ph.D. (SIB) Study Director

Sponsor (Sherex)

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Appendix B

Format for Primary Irritation Style 20





Two Test Sites



#3

Three Test Sites



Four Test Si

(19)

SKEREX

'EREX CHEMICAL COMPANY, INC.

SUBSIDIARY OF SCHERING AG, WEST GERMANY

5777 FRANTZ ROAD • P.O. BOX 646

DUBLIN. OHIO 43017

TEL (614) 764-6500

3063.12 581.019.3063

October 26, 1981

Dr. Richard Hiles
Springborn Institute for Bioresearch
Spencerville, Ohio 45887

Dear Richard:

You will be receiving under separate cover from Procter & Gamble a sample of Varisoft 222-90 Lot V2010225.

Please initiate a modified Buehler guinea pig sensitization study on this sample according to the attached protocol.

As indicated on the protocol, Elvin Newmann of Procter & Gamble will establish test concentrations, etc.

Very truly yours,

Robert L. Harrison Manager of Regulatory

Affairs

RLH/dj

Enc.

Dr. Richard Hiles Springborn Institute for Bioresearch Inc. 553 N. Broadway Spencerville, OH 45887

Dear Dr. Hiles:

Accompanying this note is a sample of Varisoft 222, lot V2-010225 which Sherex Chemical, Inc. (R. L. Harrison) has requested that we send you. Please handle it according to Mr. Harrison's requests. If you have questions, please call Mr. Harrison, Sherex Chemical Company, at 614-764-6559.

Sincerely,

D.J. Kitho

D. J. Kitko

TA recented

(21)

Study No. 3063.12

2 December 1981

SPENCERVALLE OF PHONE 419 647 419

· G., 10:

. 00036

Dr. R. L. Harrison Sherex Company 5200 Blazer Parkway Dublin, OH 43017

Study: 3063.12

Test Article: Varisoft 222-90

Lot V2010225

Confirmation of Telephoned Instructions

Additional Irritation Evaluation using four guinea pigs:

Levels: 2.5% w/v in Acetone

1.0% w/v in Acetone 0.5% w/v in Acetone 0.25% w/v in Acetone

Add \$200.00

Please sign and return one copy.

Sincerely,

SPRINGBORN INSTITUTE FOR

BIORESEARCH, INC.

A Member of SPRINGBORN GROUP, INC.

Richard A. Hiles, Ph.D.

Vice President and Director

Acute and Subchronic Toxicology

RAH: amb

R. L. Harrison

Date

cc: E. A. Newmann (Procter & Gamble)

- PG

QA

Study No. 3063.12

(22)

00038

Dr. R. L. Harrison Sherex Company 5200 Blazer Parkway Dublin, OH 43017

Study: 3063.12

Test Article: Varisoft 222.90

Confirmation of Telephoned Instructions

Additional Irritation Evaluation using four guinea pigs:

2.5% w/v in Acetone Levels: 1.0% w/v in Acetone

Add \$200.00

Please sign and return one copy of this letter.

Sincerely,

SPRINGBORN INSTITUTE FOR BIORESEARCH, INC. A Member of SPRINGBORN GROUP, INC.

Richard A. Hiles, Ph.D.

Vice President and Director

Acute and Subchronic Toxicology

R. L. Harrison

Date

RAH: amb

cc:

QA

E. A. Newmann, Procter & Gamble

SPRINGBORN GR

JAN 1 1 (23)

Study No. 3063.12

SPRINGBORN INSTITUTE FOR BIORESEARCH, INC.

SPENCERVILLE 0410 43687
PHONE 410 647-4196

4 January 82

Mr. Robert L. Harrison Sherex Company 5200 Blazer Parkway Dublin, OH 43017

RE: 3063.12

Dear Mr. Harrison:

As per our telephone conversation of January 4, 1982, we will rechallenge the guinea pig induced with Varisoft 222-90 Lot V2010225 as follows:

2.5% w/v Varisoft 222-90 in water.

5% w/v Quat A in 95% ethanol (from 3063.11)

0.5% w/v 1208-05 in 95% ethanol. (from 3063.8, .9, .10)

There will be an additional charge of \$400.00. This charge includes the extended holding time between the challenge and the rechallenge.

Please sign and return one copy for our files.

Sincerely,

SPRINGBORN INSTITUTE FOR

BIORESEARCH, INC.

A Member of SPRINGBORN GROUP, INC.

Richard A. Hiles, Ph.D.

Vice President and Director

Acute and Subchronic Toxicology

Date

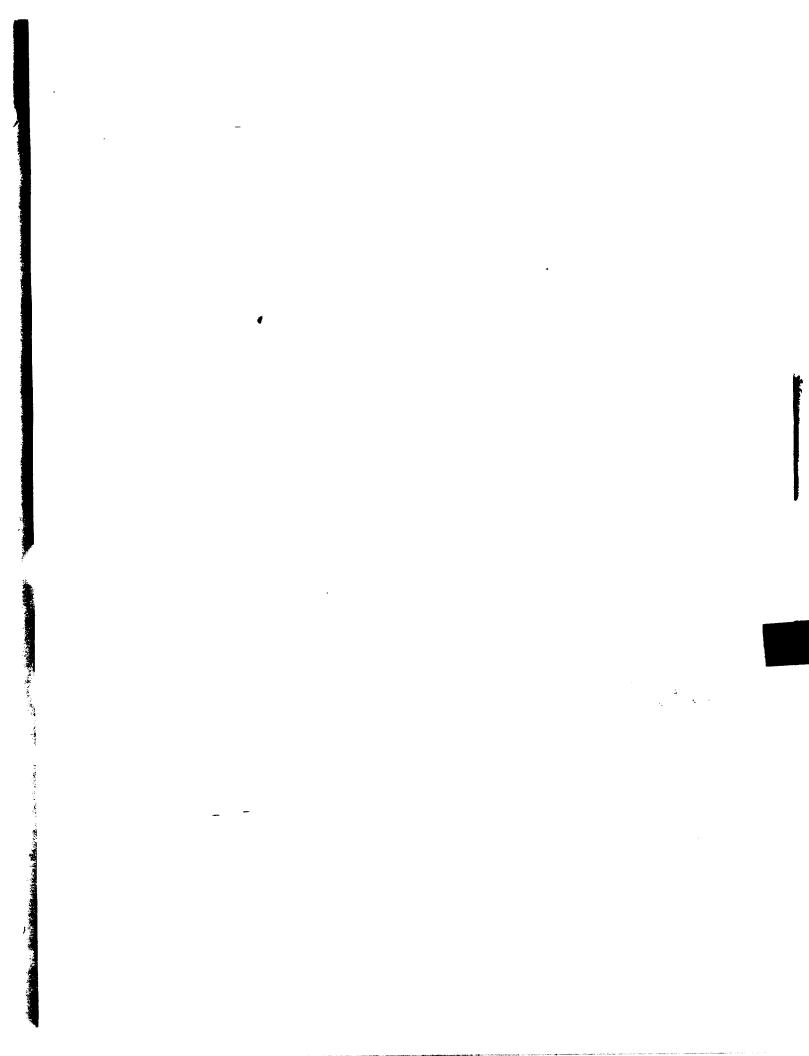
RAH: 11

cc: Accounting

PG

QA-CSD

SPRINGBORN GROUP



Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

Attachment 20:

Raltech Reports Nos. 816078, 816079, 856938, 856939, 856940, 877521, & 877522 - Skin Sensitization [PEQ 68410-69-5]

Other Raitech Scientific Services Laboratories: St. Louis MO

ATT #20 Gray Summit MO

P.O. Box 7545 • Madison, Wisconsin 53707 • 606/241-4471 A Division of Raiston Purina Company

REPORT

B.L. HARRISON SHEREX CHEMICAL COMPANY, INC. P.O. BOX 646 DUBLIN, OH 43017

RT LAB NO. 816078

ENTERED 11/13/80

REPORTED 04/02/81

VARISCET 222-90%: LOT #V2010315

PURCHASE ORDER NUMBER 020-48946 & 53

ENCLOSED:

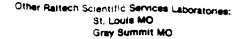
GUINEA PIG SENSITIZATION - HETHOD, SUMMARY

RAW DATA ATTACHED

GARY W. THOMPSON, BS

HEAD, ACUTE TOXICOLOGY

BY AND FOR RALTECH SCIENTIFIC SERVICES, INC.





P.O. Box 7545 • Medison, Wisconsin 53707 • 608/241-4471

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ST LAB NUMBER 816078

PAGE 2

VARISCET 222-90%: LOT #V2010315

SKIN SENSITIZATION

TEST ANIMAL: FOURTEEN MALE ALBINO GUINEA PIGS OF THE HARTLEY STRAIN, WEIGHING BETWEEN 460 AND 514 GRAMS, WERE USED FOR THIS STUDY. THE ANIMAL WERE INDIVIDUALLY HOUSED IN SCREEN BOTTOM CAGES IN A TEMPERATURE AND HUMIDITY CONTROLLED ROOM, PROVIDED CONTINUOUS ACCESS TO COMMERCIAL LAB-ORATORY FEED AND WATER AND HELD FOR AN ACCLIMATION PERIOD OF AT LEAST SEY DAYS. EACH ANIMAL WAS IDENTIFIED BY AN ANIMAL NUMBER AND CORRESPONDING EAR TAG. THE ACCLIMATED ANIMALS WERE DIVIDED INTO TWO GROUPS CONSISTING OF A NAIVE, UNTREATED CONTROL GROUP OF FOUR GUINEA PIGS AND A TREATED GRO OF TEN GUINEA PIGS.

PREPARATION OF TEST MATERIAL: TO PREPARE A 1% WEIGHT TO VOLUME MIXTURE. 1.00 G OF THE TEST MATERIAL WAS WEIGHED INTO AN ERLENHEYER FLASK. STERIL 0.9% SALINE WAS ADDED TO MAKE A TOTAL VOLUME OF 100 ML.

THE DOSAGE LEVEL WAS SELECTED BASED UPON RESULTS OBTAINED FROM A RANGE FINDING STUDY UTILIZING CONCENTRATIONS OF 1.0%, 10%, 25%, 50%, 75% AND 100% A/V MIXTURES OF TEST MATERIAL IN STERILE 0.9% SALINE.

TREATMENT: PRIOR TO EACH APPLICATION THE HAIR WAS REMOVED FROM THE BACK OF EACH ANIMAL WITH ELECTRIC CLIPPERS. THE TEST MATERIAL WAS APPLIED TO ONE AREA ON EACH ANIMAL BY PLACING 0.5 ML OF THE 1% W/V MIXTURE OF TEST MATERIAL ON A WEBRIL FAD (7/8 INCH X 1 INCH) AND PLACING THE PAD ON THE TEST SITE ALONG THE MIDLINE OF THE BACK. THE PATCH WAS COVERED WITH REMAINED IN PLACE FOF A PERIOD OF SIX HOURS AT WHICH TIME IT WAS REMOVED.

THE TEST GROUP ANIMALS RECEIVED THREE APPLICATIONS PER WEEK FOR THREE WEEK FOR A TOTAL OF NINE APPLICATIONS.

TWO WEEKS FOLLOWING THE ADMINISTRATION OF THE NINTH SENSITIZING DOSE, A CHALLENGE DOSE OF 0.5 ML OF A 1% WEIGHT TO VOLUME MIXTURE OF THE TEST MATERIAL IN STERILE 0.9% SALINE WAS ADMINISTERED TO THE TEST GROUP IN THE SAME MANNER AS DURING THE SENSITIZING PHASE OF THE STUDY. AT THIS TIME, A GROUP OF FOUR NAIVE (PREVIOUSLY UNTREATED) CONTROL ANIMALS WAS ALSO TREATED WITH THIS CHALLENGE DOSE.



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PI LAF NUMBER 816078

VARISOFT 222-90%: LOT #V2010315

PAGE 3

SKIN SENSITIZATION (CONTINUED)

OBSERVATIONS: THE APPLICATION SITES WERE READ AND SCORED FOR ERYTHENA AND EDEMA AT 24 AND 46 HOURS FOLLOWING EACH APPLICATION ACCORDING TO THE DRATECHNIQUE.* REACTIONS TO THE CHALLENGE DOSE WERE READ AND SCORED AT 24 HOURS AS WAS DONE FOLLOWING THE SENSITIZING APPLICATIONS. THE ANIMAL WERE OBSERVED FOR GENERAL BEHAVIOR AND APPEARANCE ONCE DAILY DURING THE ENTIRE STUDY PERIOD. BODY WEIGHTS WERE TAKEN AT STUDY INITIATION AND ATWEEKLY INTERVALS DURING THE STUDY.

PATHOLOGY: AT STUDY TERMINATION ALL ANIMALS WERE EUTHANATIZED AND DISCARD

SENSITIZATION RATINGS

SENSITIZATION RATE

10 - 30%

40 - 70%

80 - 100%

CLASSIFICATION
WEAK SKIN SENSITIZER
MODERATE SKIN SENSITIZER
STRONG SKIN SENSITIZER

*DRAILE, J.H., 1965, APPRAISAL OF THE SAFETY OF CHEMICALS IN FOODS, DRUGS AND COSMETICS - DERMAL TOXICITY. ASSOCIATION OF FOOD AND DRUG OFFICIALS OF THE U.S., TOPEKA, KANSAS, PP. 49-51.



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RT LAP YMMBER - 816078

VARISOFT 222-90%: LOT #V2010315

PAGE 4

SKIN SENCITIZATION (CONTINUED)

TEST ANIMAL: GUINEA PIGS

SOURCE: DEAN DAUL, LUXEMBURG, NI

DATE ANIMALS RECEIVED: 1/16/81

DATE TEST STARTED: 1/26/81

DATE TEST COMPLETED: 3/1/81

SUMMARY OF SKIN REACTIONS**

TEST GROUF: VARISOFT 222-90% LOT NO. V2010315, 1% W/V
SENSITIZING PHASE
NINE APPLICATIONS
CHALLENGE PHASE
SINGLE APPLICATION

| ANIMAL | | (0.5 | 11 1.) | | (0.5 ML) | | | | |
|--------------|--------------|--------|---------|--------|----------|--------|------|-------|--|
| | ERY | THEMA | EI | EMA | rnv. | MUDKA | | | |
| NUMBER | AVE. | (HIGH) | AVE. | | | THEMA | ED | EMA | |
| 64100001 | 0.4 | (2) | 0.3 | (HIGH) | AVE. | (HIGH) | AVE. | (HIGH | |
| 64100002 | 0.9 | (2) | | (2) | 0.0 | (0) | 0.0 | (0) | |
| 64100003 | | | 0.6 | (2) | 0.0 | (0) | 0.0 | (0) | |
| - | 1.1 | (3) | 0.7 | (2) | 0.0 | (0) | 0.0 | - | |
| 64100004 | 0.6 | (2) | 0.1 | (1) | 0.0 | - · | | (0) | |
| 64100005 | 0.1 | (1) | 0.0 | (0-) | | (0) | 0.0, | (0) | |
| 6410000ã | 0.0 | (0) | 0.0 | - | 0.0 | (0) | 0.0 | (0) | |
| 54100007 | | - | | (0) | 0.0 | (0) | 0.0 | (0) | |
| 64100008 | 0.3 | (1) | 0.3 | (1) | 0.0 | (0) | 0.0 | (0) | |
| · | 0.5 | (1) | 0.2 | (1) | 0.0 | (0) | • | | |
| 64100009 | 0.3 | (1) | 0.1 | (1) | | • | 0.0 | (0) | |
| 64100010 | 0.2 | (1) | 0.1 | · • | 0.0 | (0) | 0.0 | (0) | |
| | 3 4 2 | ` ' ' | 0 - 1 | (1) | 0.0 | (0) | 0.0 | (0) | |

NAIVE (UNTREATED) CONTROL: (CHALLENGE DOSE - VARISOFT 222-90%

| 64100011 | _ | W/Y) | | | | | | |
|----------|----|------|---|---|-----|------|-----|-----|
| 64100012 | | - | - | - | 0.0 | (0) | 0.0 | (0) |
| 64100012 | - | - | - | - | 0.0 | (0) | 0.0 | (0) |
| | - | - | - | - | 0.0 | (0) | 0.0 | (0) |
| 64100014 | •• | - | - | - | 0.0 | ~(o) | 0.0 | (0) |

**THE AVERAGE ERYTHEMA AND EDEMA VALUE IS THE MEAN SCORE FOR THE 18 OBSERVATIONS (SENSITIZING TREATMENT) OR TWO OBSERVATIONS (CHALLENGE TREATMENT) OF THE APPLICATION SITE FOR EACH ANIMAL. THE HIGH READING IS THE HIGHEST SCORE RECORDED FOR THE RESPECTIVE ANIMAL DURING THAT PHASE OF THE STUDY.

Other Gaiteon Scientific Services Laboratories: St. Louis MO Gray Summit MO

3707 • 608/241-4471

Company

PAGE 5

" #V2010315

(CONTINUED)

SD AFFEARANCE: ALL OF THE GUINEA PIGS USED IN THIS STUDY THROUGHOUT THE STUDY PERIOD. NORMAL BODY WEIGHT GAINS BE ALL ANIMALS DURING THE COURSE OF THE STUDY.

ISCFT 222-90 LOT NO. V2010315, 1% W/V): NINE OF THE TVED WITH SLIGHT TO MODERATE ERYTHEMA REACTIONS DURING ASE OF THE STUDY. SLIGHT TO MODERATE EDEMA REACTIONS Y EIGHT ANIMALS FOLLOWING THE SENSITIZING APPLICATIONS. 64100006) DID NOT EXHIBIT ANY ERYTHEMA REACTION AND TWO 100005 AND 64100006) DID NOT EXHIBIT ANY EDEMA REACTIONS TIZING PHASE OF THE STUDY.

MLS IN THE TEST OR NAIVE CONTROL GROUP EXHIBITED EITHER
DEMA RESPONSE TO THE TEST MATERIAL FOLLOWING THE CHALLENGE
0.5 ML OF A 1.0% W/V MIXTURE OF TEST MATERIAL IN STERILE

T MATERIAL IS NOT CONSIDERED A SKIN SENSITIZER IN CLOSED PATCH TECHNIQUE.

Dermal Sensitization In Guinea Pigs - Body Weights

| - 73 | | Body Welghts | ١. |
|-----------------|---|-------------------------------|---------------------------|
| X | Test Group RT No. SNOOTS Positive Control Group NA | Vehicle Q 97. Solven | Varisoft 222 |
| 11.7 | | tenicia 17 10 . Mine Test Com | pound <u>LOT NO. V201</u> |
| ∇ | Positive Control Group _NA | Vehicle NA | (170 W/V) |
| | | 10.70 | (, /0 00/0) |

| | | | Animal | Number | | | | 7 | |
|-------|-------------|-------|---------------|--------|-------|--------------|--------|-----------------|------------|
| 6410- | 6410- | 6410- | 6410. | 6410- | 6410- | 6410- | 10410- | <u> </u> | T |
| 0001 | 0002 | ∞3 | 0004 | 0005 | 0006 | 0007 | 8000 | Tech- nician | Dat /98 |
| 473 | 477 | 514 | 503 | 488 | 500 | 460 | 477 | NON SU | + |
| 525 | 572 | 562 | 560 | 550 | 538 | 512 | 520 | OFF | 2/2 |
| 584 | 550 | 433 | 651 | 625 | 1013 | 578 | 590 | NA | 219 |
| 659 | 591 | 687 | 7 <i>a</i> -3 | 682 | 668 | 620 | 634 | Sw | 2/16 |
| 741 | 643 | 750 | 810 | 768 | 742 | 691 | 705 | N20 | 3/23 |
| | | | | | | - | | | |

| | | Animal Number | | |
|-------|-------|-------------------------|-----------------|--------------|
| 6410- | 6410- | | | T |
| 0009 | 0010 | · | Tech- nician | Date /98/ |
| 508 | 510 | Scale Used: K-Tron 4809 | NIN SW | |
| 578 | 562 | Scale Used: K-Trun 4809 | CO JP | 2/2 |
| 6710 | 629 | Scale Used: 4- FON 1809 | 200 | 219 |
| 672 | 681 | Scale Used: K-Tran 4809 | Sw Sw | 2/16 |
| 743 | 758 | Scale Used: Pena 3728 | NS | 2/23 |
| | | Scale Used: | | |

| | Test Group: | RT No. 816078 | Vehicle (| 9% Saline Sterile | Test Vanso Material LOT N | 41 222 0. 4201 |
|----------|------------------|---------------|-----------|----------------------|------------------------------|-------------------|
| NA | Positive Control | | _ Vehicle | NA | Animal No. C | 2001 |
| | imal Received | | _ | . 1 | Date Initiated | 1/20 |
| Source _ | yean Dau | 1 Sex | | Ct. | allenge Date | 2/27 |

| | | | , | | e | 20 | 1 |
|------------------------------|-------------------|-------------------------------------|----------|-------|-------------|-------------|------|
| Sensi- tizing Dose No. | Dose ¹ | Obser- vation Period (Hrs) | Erythema | Edema | Technic (a) | Recorded By | Date |
| | 0.5 | . NA | NA | NA | нн | нн | 1 |
| (| | 24 48 | . 0 | 0 | - Sw | المركز ا | 1/27 |
| | 0.5 | NA | NA NA | NA. | NO | NUR | 1/28 |
| 2 | | 24 48 | 00 | 0 0 | HH | HH | 1/29 |
| 3 | 0.5 | NA NA | NA | NA. | Sw | Sw | 1/30 |
| <u> </u> | | 24 48 | 9 | 8 | Co | 100 | 1/8/ |
| /1 | 0.5 | NA | NA. | NA | JP. | 1 JP | 3/2 |
| + | | 24 48 | 8 | 0 | NA NDQ | NH | 2/3 |
| 5 | 0.5 | NA | NA NA | NA NA | HH | нн | 2/4 |
| 5 | | 24 48 | 0 | 0 | NLXI SG | ALXI So | 2/5 |

a - Dosage applied by technician indicated
 NA - Not Applicable

| Test Group: | RT No. 816078 | Vehicle O. | 3% Saline Sterile | Material LOT A | 10. 42010. WIV) |
|----------------------|---------------|-------------|----------------------|------------------------|--------------------|
| NA Positive Control | | _ Vehicle _ | NA | 6410 - Animal No. (| 1000 |
| Date Animal Received | | | | Date Initiated | |

| | | | · | | Tec | Rec | |
|------------------------------|---------------------------|-------------------------------------|--------------|-------------|--------------------|-------------|------|
| Sensi- tizing Dose No. | Dose [±] (mi) | Obser- vation Period (Hrs) | Erythema | Ed ema | <u>Technic tan</u> | Recorded By | Date |
| 6 | 0.5 | NA | NA | NA | Sw | Sw | 2/6 |
| | | 24 | 2.0 | 1.0 | 1/20 | 140 | 2/7 |
| | | 48. | <i>ఎ</i> . 0 | <i>ఎ</i> .౦ | det | PULL | 218 |
| | 0.5 | NA | NA. | NA | R | IR | 2/9 |
| 1 | | 24 | 2.0 | 1.0 | NJA | Sw | 2/10 |
| | | 48 | 1,0 | 1.0 | Co | Co | 2/11 |
| \mathbf{Q} | 0.5 | NA | NA . | NA | حن | 56 | 2-11 |
| 0 | | 24 | 0 | 0 | Q1 190 | | 2-12 |
| | | 48 | 0 | Ö | pp | السوا | 0/13 |
| a | 0.5 | NA | NA. | · NA | M | 100 | 2/13 |
| -1 | | 24 | Ö | 0 | ни | · 14 | 2/14 |
| | | 48 | | 0 | ŚĠ | : 56 | 2-15 |
| Challenge | 0.5 | NA | NA. | NA | P | R | 2/27 |
| Dose | | 24_ | 0 | 0 | - Cheb | -mo | 2/18 |
| | | 48 | 0 | 0 | THE | dal | 3/1 |

a - Dosage applied by technician indicated
 NA - Not Applicable

| | | 1 100 | |
|---------------------------------------|--------------|------------------|---|
| Test Group: | 810018.on tr | Vehicle 0,9% Sal | Test Vanso .22 ine Material LOT Na. V20 (17. w/v) |
| NA Positive Control | | Vehicle NA | Animal No. <u></u> |
| Date Animal Received Source Dean Date | | | Date Initiated 1/20 |

| | | | | | Tecl | Rec | L |
|---|-------------------|-------------------------------------|----------|-------|-----------------------|-------------|------|
| Sensi- tizing Dose No. | Dose ² | Obser- vation Period (Hrs) | Erythema | Edema | <u>Ceclin I c Lan</u> | Recorded By | Date |
| ı | 0.5 | NA | NA | NA | HH | нн | Y26 |
| ł | | 24 | 0 | 0 | Sw | 1 Sw | 1/27 |
| | | 48. | . 6 | 0 | 45 | IJP | 1/18 |
| 2 | 0.5 | NA | NA | NA NA | NUR | NN | |
| _ | | 24 | 0 | 0 | Z Z | MM | 1/29 |
| | 1 | 48 | 0 | 0 | Sw | Sw | 1/30 |
| 3 | 0.5 | NA | AK . | NA | Sw | Sw | 1/30 |
| ے | | 24 | 1.0 | 1.0 | Co | 100 | 1/31 |
| | | 48 | 1.0 | 0 | Co | 100 | 2/, |
| 11 | 0.5 | NA. | NA | NA | R | 100 | 3/2 |
| 4 | | 24 | /.0 | 0 | | · ~* | -2/3 |
| *************************************** | | 48 | 0 | 0 | 109 | in Co | 2/4 |
| 5 | 0.5 | NA | NA | NA | 77 | # | 2/4 |
| | 1 1 | 24 | 0 | 0 | NO | | 2/5 |
| | | 48 | 1.0 | 0 | 56 | 86 | 2-6 |

a - Dosage applied by technician indicated
 NA - Not Applicable

| \boxtimes | Test Group: | 810018 on TR | Vehicle Q | 9% Saline Sterile | Test Vansa Material LOT A | zz 22.9 <u>10. Y 201</u> 0. W I Y) |
|-------------|------------------|--------------|-----------|----------------------|------------------------------|---|
| NA | Positive Control | | | | Animal No. | |
| Date Ar | nimal Received | 1/16/81 | | 1 | Date Initiated | 1/261 |

Source Dean Daul Sex 0 Challenge Date 2/27/8

| | | | | | Tech | Rec | <u> </u> |
|------------------------------|-------------------|-------------------------------------|-----------|---------------|-------------|-------------|---------------|
| Sensi- tizing Dose No. | Dose ² | Obser- vation Period (Hrs) | Erythema: | Ed ema | Technic ten | Recorded By | Date: : '/98/ |
| | 0.5 | NA | NA. | NA | 5w | Sw | 2/6 |
| م ا | | 24 | 2.0 | 2.0 | 100 | 179 | 2/7 |
| | | 48 | 20 | 2.0 | 140 | MUN | 218 |
| - | 0.5 | NA | . NA | NA | TP | JP | 2/4 |
| | | 24 | a.o □ | 1,0 | NOA | Sw | 2/10 |
| | | 48 | 1,00 | 1.0 | co | co | 2/11 |
| | 0.5 | · NA | NA | NA | ડ હ | 56 | 2-1) |
| 8 | | 24 | 1.0 | 1.0 | del | 1 12 | 2-12 |
| | | 48 | 1.00 | 1.0 | the | 150 | 2/13 |
| 9 | 0.5 | NA | NA | NA | ngo | go | 2/13 |
| | | 24. | 1.00 | 1.0 | 7474 | . HH | 2/14 |
| | | 48 | 1.0 8 | 1.0 | 56 | <u>داک</u> | کا-2 |
| Challenge | 0.5 | NA | NA NA | NA | SP | R | 2/28 |
| Dose | | 24 | 0 | 8 | del | del | |
| | | 48 | 0 | | June 1 | ورود | 3 /, |

a - Dosage applied by technician indicated

NA - Not Applicable

D = Desquamation Sw 2/10/81

| Test Group: | RT No. 816078 | Vehicle O | 9% Saline | Test Varisoft 222. Material LOT NO. V201 (1% w/v) |
|------------------------|---------------|-------------|-----------|---|
| NA Positive Control | Group NA | _ Vehicle _ | NA | 410- Animal No. 0003 |
| Date Animal Received | | | I | Date Initiated 1/26 |
| Source <u>Dean Dau</u> | <u>L/</u> Sex | | Ch | allenge Date 2/27 |

| | | | | | F . | — | 1 |
|------------------------------|-------------------|-------------------------------------|----------|--------|------------|-------------|-------|
| Sensi- tizing Dose No. | Dose ² | Obser- vation Period (Hrs) | Erythema | Ed ema | [echniclan | Recorded By |)981 |
| _ | 0.5 | NA | NA. | NA | НН | | 1/26 |
| 1 | | 24 | 0 | 0 | (4) | 150 | 1/27 |
| | ! | 48 - | .0 | 0 | ليك | 1 | ins |
| 2 | 0.5 | NA | NA | NA | NON | lus | 1/28 |
| | | 24 | 0 | 0 | HH | HH | 1/29 |
| | | 48 | 0 | 0 | Sw | سکا | 1/30 |
| 3 | 0.5 | · NA | NA . | NA | Sw | Sw | 1/30 |
| <u>ح</u> | | 24 | 0 | 0 | 00 | ao | Jer . |
| | · | 48 | 0 | 0 | | Ca | 2/, |
| د ا | 0.5 | N A | NA. | · NA | R | R | 2/2 |
| T | | 24 | 0 | ٥ | HH | えよ | 43 |
| | | 48 | 0 | 0 | NOR | Co | 2/4 |
| 5 | 0.5 | NA | NA | NA | 44 | 44 | 214 |
| | | 24 | 0 | 0 | 1/29 | | 3/5 |
| | | 48 | .0 | 0 | 56 | 50 | 2-6 |

a - Dosage applied by technician indicated
 NA - Not Applicable

| \bowtie | Test Group: | RT No. | 16078 | Vehicle O' | 9% Saline Sterile | Material LOT N | <u>0. 42010</u> wlr) |
|-----------|------------------|--------|-------|-------------|----------------------|------------------------|-------------------------|
| NA | Positive Control | | | _ Vehicle _ | NA | 0410 - Animal No. C | <u>, Econ</u> |
| | nimal Received | | | | I | Date Initiated | 1/261 |
| Source | Dean Day | L/ | Ser A | | . ~ | | 2/201 |

Varisoff 222.9

| | • | | | | | | |
|------------------------------|-------------------|-------------------------------------|-----------|-------|-------------|-------------|------------|
| | | | · | | Tec | Rec | L |
| Sensi- tizing Dose No. | Dose ² | Obser- vation Period (Hrs) | Erythema | Edema | Technic Lan | Recorded By | Date / 98/ |
| | 0.5 | NA | NA. | ná | Sw | Sw | 3/6 |
| ما | | 24 | 2.0 | 2.0 | 100 | dul | 2/7 |
| | | 48 - | 3.0 A | ء. ٥ | 770 | INUN | 2/8 |
| _ | 0.5 | NA. | NA | NA | P | P | 2/9 |
| (| | 24 | NA 2.0 | 2,0 | NOW | Seu | 2/10 |
| · | 1 | 48 | 2. O D | 2-0 | Co | Co | 2/11 |
| C | 0.5 | · NA | NA | na | <i>5</i> 6 | 56 | 2-11 |
| 8 | | 24 | 32000 | 2.0 | del | 1 18 | 2-12 |
| • | • | 48 | 2.00 | 1.0 | 140 | اسكا | 2/13 |
| \circ | 0.5 | NA NA | NA. | NA | M | 1 mg | 2/13 |
| 9 | 1 1 | 24 | 2.0 | 1.0 | HH | · +++ | a//4 |
| | | 48 | 2.0 | 1.0 | <u>ئ</u> خ | 56 | 2-15 |
| Challenge Dose | 0.5 | NA | NA | NA | R | R | 2/27 |
| DOZE | 1 1 | 24 | 0 | 0 | de | 130 | 2/28 |
| | 1 | 48 | 0 | 0 | mo | de | 3/1 |

a - Dosage applied by technician indicated
 NA - Not Applicable

A = Subcutanions hemorrhage 218181 NA

D = DESQUAMATION CO 2/11/8/ C = set acab formation 42 2/12/8/ Oriending evalure 2/12/8/

| \boxtimes | Test Group: | RT No. | <u>810018</u> | Vehicle Q | .9% Saline Sterile | Test Vans. Material LOT A | 70. ¥2010 |
|-------------|------------------|-----------|---------------|-----------|-----------------------|------------------------------|-----------|
| NA | Positive Control | | | _ Vehicle | NA | Animal No. | 1004° |
| Date An | nimal Received | 1/16 | /81 | | Ī | Date Initiated | 1/261 |
| Source | Dean Day | <u>L/</u> | Sex O | | Ch | allenge Date | 2/27/ |

| mi) | Obser- | | | Technic (a) | [0] | |
|--------|--------------|--|---|---|---|---|
| | Period (Hrs) | Erythema- | Edema | | Recorded By | 10/8/ |
| 5 | NA | МА | NA | HH | нн | 1/26 |
| | 24 48 | 0 | 0 | FU. | LEW YEL | 1/27 |
|),5 | NA | NA. | NA NA | NIR | 1 NOO | 1/28 |
| | 24 48 | D | 0 | HW. | HH | 1/29 |
|).5 | | • | | | | 1/30 |
| | 24 48 | 2.0 | 1.0 | Co | 100 | 1/91 |
| .5 | NA | NA. | · NA | | | 2/1 |
| | | 7.0 | 0 | HW | こま | 2/3 |
| 5 | | | 0 | AN | (2) | 2/4 |
| | NA | NA | NA NA | 44 | 144 | 2/4 |
|) } | .5 | 24 48 .5 NA 24 48 .5 NA 24 48 | 24 0 48 0 .5 NA NA 24 2.0 48 2.0 5 NA NA 24 1.0 48 0 | 24 0 0 0 48 0 0 .5 NA NA NA 24 2.0 /.0 48 2.0 0 .5 NA NA NA 24 /.0 0 48 0 0 | 24 0 0 HM 48 0 0 SW .5 NA NA NA SW 24 2.0 /0 30 48 2.0 0 CO 5 NA NA NA NA JR 24 /.0 0 HM 48 0 0 HM | 24 0 0 HM HM 48 0 0 5W 5W 5 NA NA NA SW 5W 24 2.0 1.0 0 0 0 0 0 48 2.0 0 0 0 0 0 5 NA NA NA NA TR TR 24 1.0 0 0 HM HM 48 0 0 ADA CO |

a - Dosage applied by technician indicated

NA - Not Applicable

| Test Group: | RT No. 816078 | Vehicle 0,9% Saline Sterile | Test Varisoft 222.9 Material LOT NO. 42010 (1% wlv) |
|----------------------|---------------|-----------------------------|---|
| NA Positive Control | | Vehicle NA | |
| Date Animal Received | 1/16/81 | - | Date Initiated 1/26/ |
| Source Dean Day | دا Sex | · | hallenge Date 2/27/ |

| | | | | | Tech | Rec | |
|------------------------------|-------------------|-------------------------------------|----------|--------|--------------------|-------------|--------------|
| Sensi- tizing Dose No. | Dose ² | Obser- vation Period (Hrs) | Erythema | Ed ema | <u>Cecimic Lan</u> | Recorded by | Date 1981 |
| . , | 0.5 | NA | NA | NA. | 5w | Sw | 2/اد |
| 6 | | 24 | 0 | 0 | 1279 | 100 | 2/7 |
| | | 48 | - 0 | 0 | ay | PCVI | 218 |
| | 0.5 | NA | NA | NA | SP | SP | 2/9 |
| / | | 24 | 0 | 0 | NJA | Sw | 2/10 |
| | | 48 | 0 | 0 | CO | Co | 2/11 |
| C | 0.5 | . NA | NA | _ NA | SG | 156 | 2-11 |
| 1 X | | 24 | 1.0 | 0 | 140 | 1 JR | 2-12 |
| . 0 | 1 | 48 | 1.0 | 0 | JAD . | التكا | 2/13 |
| | 0.5 | NA | NA. | . NA | Top | cht | 2/13 |
| 1 4 | | 24 | 1.0 | 0 | | . 44 | 2/14 |
| | | 48 | 1,0 | 0 | ŚĠ | So | 2-15 |
| Challenge Dose | 0.5 | NA | NA | NA | P | TP | 2/2 |
| Dose | | 24 | 0 | 0 | she | Jun - | -/28 |
| 1 | | 48 | Q | 0 | 2300 | del | 3/1 |

a - Dosage applied by technician indicated
 NA - Not Applicable

| \bowtie | Test Group: | RT No. 816078 | _ Vehicle O | 9% Saline Sterile | Material LOT N | 0. Y201 |
|-----------|------------------|---------------|-------------|----------------------|----------------|---------|
| NA | Positive Control | | Vehicle | NA | Animal No. | 005 |
| | nimal Received | | - | I | Date Initiated | 1/26 |
| Source | Dean Dau | L/ Sex | | ٠ | -11 | 2/20 |

| | | | | | Tecl | Rec | L |
|------------------------------|-------------------|-------------------------------------|----------|-------|-------------|-------------|-----------|
| Sensi- tizing Dose No. | Dose ² | Obser- vation Period (Hrs) | Erytheme | Edema | Cechnic Lan | Recorded By | Date 1981 |
| . , | 0.5 | NA | NA | NA | HH | нн | 1/26 |
| | 1 | 24 48 · | 0 | 10 | Sw | 150 | 1 /27 |
| | + | 40. | 0 | 10 | 1 7 | <u> </u> | 1/28 |
| 2 | 0.5 | NA | NA NA | NA | 11000 | no | 1/28 |
| _ | 1 + | 24 | C | 0 | HH | NH | 1/29 |
| | 0.6 | 48 | 0 | 0 | Sw | Sw | 1/30 |
| .3 | 0.5 | . NA | NA | NA | Sw | اسك | 1/30 |
| | 1. | 24 | 0 | 0 | Co | 100 | 1/2 |
| | - | 48 | 0 | 0 | Co | 100 | 2/1 |
| 4/ | 0.5 | NA. | NA' | NA. | SP | JA | 2/2 |
| 7 | | 24 | 0 | ට | NH | ·HH | 223 |
| | | 48 | 0 | 0 | 100 | Co | 2/4 |
| 5 | 0.5 | NA | NA | NA. | 11 | H H | 2/4 |
| <u> </u> | | 24 | | 0 | IN | RUN | 2/5 |
| | <u> </u> | 48 | 0 | 0 | <i>ی</i> خ | ا ماک | 2-6 |

a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Test Vansoft 222-96

Test Group: RT No. 816078 Vehicle 0.9% Saline Material LOT NO. V2010:

Sterile (17-w/v)

NA Positive Control Group NA Vehicle NA Animal No. 0005'

Date Animal Received //16/81

Source Dean Daul Sex O Challenge Date 2/27/8

Sensi-Obser-Doseª tizing vation. Erythema Edema Period Dose No. (mi) 1981 (Hrs) 0.5 2/6 NA NA NA 24 1.0 48. 0.5 NA NA NA 24 2/10 0 48 CO 0.5 NA NA NA 24 1.0 48 -0.5 NA NA NA 24 48 ی 56 0.5 hallenge NA NA NA pp 2/28 the 24 D05e 48

a - Dosage applied by technician indicated

NA - Not Applicable

| Test Group: | RT No. 816078 | Vehicle 0,9% S | aline Material LOT NO. V201 Te (17. WIV) |
|------------------------|---------------|----------------|---|
| NA Positive Control | | _ Vehicle | 9 Animal No. 000 (|
| Date Animal Received | | | Date Initiated 1/26 |
| Source <u>Dean Dau</u> | L/ Sex | • | Challenge Date 2/27 |

| | | | | | Tec | Re | |
|------------------------------|-------------------|-------------------------------------|----------|-------|-------------|-------------|-------|
| Sensi- tizing Dose No. | Dose ² | Obser- vation Period (Hrs) | Erythema | Edema | Technic Lan | Recorded By | 1981 |
| | 0.5 | na | NA | NA | ни | 1111 | الجده |
| l | | 24 48 | O | 10 | Sw | 15W | 1/27 |
| 7 | 0.5 | NA | NA NA | NA NA | NUN | wo | 1/28 |
| Z | | 24 48 | 0 | 00 | HH | HH | 1/29 |
| 2 | 0.5 | NA NA | na | NA | Sw Sw | لتكا | 1/30 |
| 3 | | 24 48 | 0 | 00 | 00 | 100 | 1/85 |
| 41 . | 0.5 | NA. | NA. | NA | R | 137 | 2/2 |
| Τ | | 24 | O | 0 | HH AUN | . HH | 2/3 |
| 5 | 0.5 | NA | NA NA | NA NA | HH | 17H | 2/4 |
|) | | 24 48 | <u> </u> | 0 | 1179 56 | | 2-6 |

a - Dosage applied by technician indicated
 NA - Not Applicable

| Test Gro | oup: RT No. 816078 | Vehicle 0.9% Salin Sterile | Test Varisoft 222.9 Material LOT NO. 42010 (1% WIV) |
|-------------|-----------------------------|-------------------------------|---|
| NA Positive | Control Group NA | Vehicle | Animal No. 000 Lo |
| | eived //16/81 Daul Sex O | | Date Initiated 1/26/ Challenge Date 2/27/ |

| | | | | | Tecl | Rec | L |
|------------------------------|--|-------------------------------------|----------|---------|-------------|-------------|--------|
| Sensi- tizing Dose No. | Dose ² | Obser- vation Period (Hrs) | Erythema | . Edema | Technic Lan | Recorded By |) 198/ |
| . , | 0.5 | NA | NA | NA | Sw | Sw | 2/6 |
| 6 | | 24 48 | 0 | 0 | N | m | 2/2 |
| | | 40. | - 0 | 10 | 1 pp | NZO | 2/8 |
| 7 | 0.5 | NA | NA | NA | R | 12 | 3/9 |
| / | 1 | 24 | 0 | 0 | NON | Sw | 2/10 |
| | | 48 | 0 | 0 | Co | Co | 2/11 |
| | 0.5 | . NA | AK | NA | 56 | SG | 2-11 |
| 8 | | 24 | 0 | 0 | 140 | JE | |
| 0 | <u> </u> | . 48 | | 0 | M | Sw | 2/13 |
| 0 | 0.5 | N A | NA | NA | art | 200 | 2/13 |
| 9 | | 24 - | | 0 | HH | 141 | 2/14 |
| <u>'</u> | | 48 | | | SG | یاک | 2-15 |
| Challenge | 0.5 | NA | NA NA | NA | R | 35 | 2/27 |
| Dose | 1 [| 24 | 0 | 0 | dil | m | 2/28 |
| | <u> </u> | 48 | | 0 | 130 | de | 3/1 |

a - Dosage applied by technician indicated
 NA - Not Applicable

| Test Group: | RT No. 816078 | _ Vehicle O. | 3% Saline Sterile | Test Vans Material LOT A | 10. 42010 |
|----------------------|---------------|--------------|----------------------|-----------------------------|-----------|
| NA Positive Control | | Vehicle _ | NA | Animal No. | 007 |
| Date Animal Received | | | r | ate Initiated | 1/26/ |
| Source Dean Day | L/ Sex | • | Ch | allenge Date | 2/27/ |

| | | | | | Tech | Rec | |
|------------------------------|---------------------------|-------------------------------------|----------|-------|-------------|-----------------|----------|
| Sensi- tizing Dose No. | Dose ² (mi) | Obser- vation Period (Hrs) | Erythema | Edema | Technic Lan | Recorded By | Date /OS |
| , | 0.5 | NA | NA | NA | НН | | 1/20 |
| / | | 24 | 0 | 0 | | 181 | 1/27 |
| | | 48 | 0 | 0 | ليد | 1 1 | 1/18 |
| 2 | 0.5 | NA NA | NA | NA NA | NOD | 100 | 1/28 |
| 2 | 1 - | 24 | 0 | ව | エエ | 774 | 1/29 |
| • | - | 48 | | 0 | Sw | Sw | 1/30 |
| 3 | 0.5 | NA | NA . | NA | Sw | (| 1/30 |
| \mathcal{O} | | 24 | 0 | 0 | Co | 100 | 1/3/ |
| | | 48, | 0 | 0 | Co | TWA ETW WOO FIN | 24, |
| 41 | 0.5 | na' | NA. | . NA | R | 5 | 2/2 |
| . 7 | | 24 | 0 | 0 | | BUS TH | a/3 |
| | | 48 | | 0 | 100 | | 2/4 |
| 5 | 0.5 | NA | NA | NA | 7 | ` | 24 |
| | | 24 | ٥ | ٥ | wo | | 2/3 |
| | | 48 | 0 | 0 | 50 | <u>ک</u> ن | 2-60 |

a - Dosage applied by technician indicated
 NA - Not Applicable

O Recording error HH a13181

| Test Group: | RT No. 816078 | Vehicle O | 9% Saline Sterile | Test Vansa Material LOT A | of1 222 ·9 10. Y 2010 W/V) |
|------------------------|---------------|-----------|----------------------|------------------------------|---------------------------------------|
| NA Positive Control | Group NA | _ Vehicle | NA | Animal No. | 007 |
| Date Animal Received | | _ | _ | Date Initiated | · · · · · · · · · · · · · · · · · · · |
| Source <u>Dean Dau</u> | Sex O | | Ct. | nallenge Date | 2/271 |

| | _ | | | | Tech | Rec | |
|------------------------------|-------------------|-------------------------------------|----------|-------|--------------|-------------|-----------|
| Sensi- tizing Dose No. | Dose ² | Obser- vation Period (Hrs) | Erythema | Edema | Cechnic (a)) | Recorded By | Date /98/ |
| , | 0.5 | NA | NA. | NA . | Sw | Sw | 2/6 |
| LP . | | 24 | 0 | 0 | W | INP | 2/7 |
| | <u> </u> | 48. | -0 | ! 0 | de | MAN | 2/8 |
| 7 | 0.5 | NA | NA | NA | TP | P | 13/9 |
| / | | 24 | 1.0 | 0 | NDA | ليك | 2/10 |
| | | 48 | 1.0 | 1.0 | CO | 0 | 2/1/ |
| | 0.5. | : NA = | NA | NA | 56 | SG | 2-11 |
| 8 | <u> </u> | 24 | 1.0 | 1:0 | Typ | IJR | 2-12 |
| | <u> </u> | 48 | : /. 0 | 1.0 | 1 mg | Sw | 2/13 |
| \circ | 0.5 | NA | NA. | NA : | del | car ! | 2/13 |
| .7 | | 24 | 1,0 | 1.0 | 44 | . 77 | 2114 |
| | | 48 📑 | 1.0 | 1.0 | 50 | . SG | 2+13 |
| Chailenge Dose | 0.5 | NA | NA | NA | R | 157 | 2/27 |
| Dasp | | 24 | 0 | 0 | 740 | 740 | 2/28 |
| 2000 | | 48 | 0 | 0 | 141 | 130 | 3/1 |

a - Dosage applied by technician indicated
 NA - Not Applicable

Naive No. 8110078 Venicle 0.9% Saline, Sterile

| Date Animal Received | | |
|-------------------------------|----------------|---------|
| Source <u>Dean Daul</u> Sex 3 | Challenge Date | 1/20/81 |

| | | | | | Tech | Rec | 2 | |
|-------------|-------------------|------|-------------------------------------|----------|-------|------------|-------------|------|
| Animal No. | Dose ² | | Obser- vation Period (Hrs) | Erythema | Edema | Technician | Recorded By | 1481 |
| 6410- | 0.5 | NA | NA | NA | R | R | 2/27 | |
| ∞ 11 | | 24 | 0 | 0 | -hh | 72 | 2/28 | |
| 10110 | | 48 | 0 | 0 | det | 100 | | |
| 6410- | 0.5 | NA | NA. | NA. | IR | 1 | 2/27 | |
| 0012 | | 24 | 0 | 0 1 | au | 90 | 12/28 | |
| | | 48 | 0 1 | 0 | dil | del | 3/ | |
| 10- L | 0.5 | NA | NA | · NA | R | TP | 2/27 | |
| 0013 | ļ | 24 | _ 0 | 0 | Topo | 740 | 2/28 | |
| | 1 | 48 | 0 | 0 | THE | PP | 3/1 | |
| 0410- 1 | 0.5 | NA | | | R | R | 2/27 | |
| 0014 | | 24 1 | 0 | 0 | del | 190 | 1/28 | |
| | | 48 | | 0 | m | ا صرا | 3/1 | |
| | | - NA | NA | NA | | | · · · · · · | |
| 1 | L | 24 | | | | i | | |
| | | 48 | | | 1 | | | |

a - Dosage applied by technician indicated

NA - Not Applicable

Dermal Sensitization In Guinea Pigs - Body Weights

Test Group RT No. 8110078 Vehicle 0.9% Saline Test Compound LOT NO. V2010
Naive Untreated Control

Sterile

(170 W/V)

| | | | | Number | - | | | 7 | |
|-------|-------|-------|-------|--------|---|---|-------|-----------------|--------------|
| 6410- | 6410- | 6410- | 6410- | | | T | | | T |
| ∞11 | 0012 | ∞13 | 0014 | | | | | Tech- nician | Date /98/ |
| 497 | 489 | 474 | 493 | | | | | 12 | |
| 575 | | | | | - | | | WW Sw | 1/26 |
| 2/3 | 573 | 562 | 568 | | | | | 0 JF | 2/2 |
| 6666 | 645 | 458 | 648 | | | | | | 219 |
| 719 | 702 | 731 | 707 | | | | | SW | 3/16 |
| 783 | 786 | 789 | 775 | | | | | | |
| | | | | | | | | 109 | 2/23 |
| NA | NA | NA | 24 | | | | \ \ \ | 79 | NA |

| Animal Number | | |
|-------------------------|-------|------|
| · | Tech- | Date |
| Scale Used: K-Tron 4809 | NO E. | 1/26 |
| Scale Used: K-True 4809 | C P | 2/2 |
| Scale Used: K-TRON 4809 | RU | 2/9 |
| Scale Used: K-Tron 4809 | SW | 2/16 |
| Scale Used: Penn 3728 | NOO | 2/23 |
| _Scale Used: NA | NA | NA |

| Test Group: | RT No. 816078 | Vehicle 0,9 | % Saline Sterile | Test Vansa Material LOT A | of1 222.9 10. V2010 WIV) |
|-------------------------|---------------|-------------|---------------------|------------------------------|--------------------------------|
| NA Positive Control | | Vehicle | NA | Animal No. | 1010 |
| Date Animal Received | | | | Date Initiated | |
| Source <u>Seuri Cat</u> | <u> </u> | | Ch | allenge Date | 2/27/ |

| | | | • | | Tecl | Rec | |
|------------------------------|-------------------|-------------------------------------|----------|-------|--------------|-------------|-------|
| Sensi- tizing Dose No. | Dose ² | Obser- vation Period (Hrs) | Erythems | Edema | Technic (a)) | Recorded By | Date' |
| , | 0.5 | NA | NA | NA | +++ | HH | 1 |
| | | 24 | 0 | 0 | مريدك | Sw | 1/27 |
| | ! | 48 - | . 0 | 0 | 75 | 1 57 | 1/28 |
| 2 | 0.5 | NA | NA | NA | NOO | no | 1/28 |
| _ | | 24 | 0 | 0 | 太 之 | HH | 1/29 |
| | | 48 | | 0 | Sw | Sw | 1/30 |
| 3 | 0.5 | NA. | na . | NA | Sw | Sw | 1/30 |
| | | 24 | 0 | 10 | Co | 100 | 1/3 |
| | <u> </u> | 48 | 0 | 0 | Co | 100 | 2/, |
| / / | 0.5 | NA. | NA | . NA | SP | R | 2/2 |
| 7 | | 24 | 0 | 0 | 114 | 144 | 2/3 |
| | | 48 | 0 | 0 | NOD | Co | 3/4 |
| 5 | 0.5 | na | NA | NA | HH | ## | 214 |
| | | 24 | 40 | ٥ | NID | NJA | 2/5 |
| | | 48 | 1.0 | 0 | 56 | حک | 2-6 |

a - Dosage applied by technician indicated
 NA - Not Applicable

| Test Group: | RT No. 816078 | Vehicle 0.9% Saline | Test Vansofi 222.9 Material LOT NO. V2010 (1% w/v) |
|------------------------|---------------|---------------------|--|
| NA Positive Control | Group NA | Vehicle NA | Animal NoO_/_O' |
| Date Animal Received | | | Date Initiated 1/26/ |
| Source <u>Dean Dau</u> | L/ Sex | | hallenge pate 2/27/ |

| | | | • | | Tech | Rec | L |
|------------------------------|-------------------|-------------------------------------|-----------|---------|-------------|-------------|-----------|
| Sensi- tizing Dose No. | Dose ^a | Obser- vation Period (Hrs) | Erythema. | Edema | Technic Len | Recorded By | Date 198/ |
| , | 0.5 | AK | NA. | NA | Sw | Sw | 2/6 |
| | | 24 | 1.0 | 1.0 | 100 | 14 | 2/7 |
| | ļļ. | 48 - | 1.00 | 1.0 | m | PONI | |
| 7 | 0.5 | NA | NA | NA. | R | P | 2/9 |
| 1 | | 24 | 0 | 0 | NOR | Sw | 2/10 |
| | | 48 | 0 | 0 | Co | 100 | 2/11 |
| 0 | 0.5 | . NA | AM | NA | SG | 56 | 2-11 |
| X | | 24 | 0 | 0. | 140 | 1 18 | 2-12 |
| | | 48 | 0 1 | 0 | M | الكوا | 2/13 |
| 0 | 0.5 | na | NA. | NA. | · m | 190 | 2/13 |
| 7 | | 24 | 8 | 0 | 44 | 44. | 2/14 |
| · | | 48 | 0 | . 0 | | 50 | 2-15 |
| Challenge | 0.5 | NA | NA | NA | R | 17 | 2/27 |
| 4550 | | 24 | 0 | 0 | 14) | 120 | 2/28 |
| | <u> </u> | 48 | 0 | \circ | 140 | m | 3/1 |

a - Dosage applied by technician indicated
 NA - Not Applicable

D=desquamation 1/8/8/ NDA

| \boxtimes | Test Group: | RT No. | SLO918 | _ Vehicle O | 9 <u>% Saline</u> Sterile | Material LOT N | <u>io. V201</u> w/v) |
|-------------|------------------|-----------|--------|-------------|------------------------------|----------------|-------------------------|
| NA | Positive Control | | | | | Animal No. | |
| Date A | nimal Received | 1/16 | /81 | | | Date Initiated | 1/26 |
| Source | Dean Day | <u>./</u> | Sex | | · c | hallenge Date | 2/27 |

| Sensi- tizing Dose No. | Dose ¹ | Obser- vation Period (Hrs) | Erythema | Edema | Cechnic Lan | Recorded By | 198) |
|------------------------------|-------------------|-------------------------------------|-----------|-------|-------------|--------------------|---------------------|
| | 0.5 | NA | NA NA | NA | HH | 44 | 1/24 |
| 1 | | 24 | 0 | 0 | Sw | Sw | 1/27 |
| ′ | | 48. | . 0 | 1 0 | 000 | 1 3 m | 1/18 |
| | 0.5 | NA | NA. | NA. | NO | NJO | 1/28 |
| 2 | | 24 | 0 | 0 | エナ | 117 | 429 |
| <u> </u> | | 48 | 0 | 0 | ريبك | Sw | 1/30 |
| 2 | 0.5 | · NA | na | NA | Sw | 5w 60 Cs | 1/30 1/8/ 2/, |
| 3 | | 24 | 0 | 0 | Co | 100 | 1/8/ |
| | | 48 | 0 | 0 | CO | 1 Co | 2/1 |
| , / | 0.5_ | NA . | NA | NA | R | F | 3/2 |
| :7 | | 24 | 0 | 0 | 1111 | HH: | 4/3 |
| | <u> </u> | 48 | . 0 | 0 | NON | Co | 2/4 |
| 5 | 0.5 | NA | МА | NA | 44 | HH | 2/4 |
| | | 24 | 0 | | NY | NJO | <i>کاح</i> |
| | I F | 48 | 0 | ٥ | 50 | 56 | 2-6 |

a - Dosage applied by technician indicated
 NA - Not Applicable

| | Test Group: | KI NO. 8100.18 | _ Vehicle O. | 7/0 Sovine Sterile | Material LOT NO. V | 201 v) |
|---------|------------------|----------------|--------------|-----------------------|--------------------|-----------|
| NA | Positive Control | | Vehicle | NA | | 9 |
| Date Ar | nimal Received | 1/16/81 | | 1 | Date Initiated | 26 |
| Source | Dean Day | دا Sex _ ح | | G | nallenge Date 2/ | 27 |

| | | | • | | Tech | Rec | L |
|------------------------------|-------------------|-------------------------------------|---------------|-------|-------------|-------------|--------------|
| Sensi- tizing Dose No. | Dose ² | Obser- vation Period (Hrs) | Erythema | Edema | Technic Lan | Recorded By | Date 1981 |
| 6 | 0.5 | na - | NA | NA | Sw | Sw | 2/6 |
| | | 24 | 0 | 0 | 1170 | 100 | |
| | | 48 | . 0 | | July . | DUN | 2/8 |
| 1 | 0.5 | NA | NA · | NA | 3 | F | 2/9 |
| / | 1 4 | 24 | 1,0 | 0 | 1/20 | Sw | 2/10 |
| | <u> </u> | 48 | 1.0 | 0 | Co | Co | 2/11 |
| C. | 0.5 | NA - | NA | NA | SO | 150 | 2-11 |
| 8 | | 24 | 1.0 | 1.0 | del | 1 JR | 2-12 |
| | | 48 | 1.00 | 0 | 199 | ليك | 2/,3 |
| | 0.5 | NA - | NA | NA | Art. | an! | 2/13 |
| .9 | | 24 | 1,00 | 0 | 14 | エオ・ | 2/14 |
| - | | 48 | Δ [0] | 0 | 56 | یک | 2-15 |
| Challenge | 0.5 | NA | NA | NA. | R | TP | 3/27 |
| DOSE | 1 | 24 | 0 | 0 | 140 | m | 2/18 |
| | 1 | 48 | \mathcal{O} | 0 | M | 740 | 3/1 |

a - Dosage applied by technician indicated
 NA - Not Applicable

D=Desquamation 5w 2/13/8/

| | DERMAL S | SENSITIZATION STUDY | IN GUINEA | PIGS | Vania att 222 |
|----|------------------|---------------------|-------------|----------|--|
| | Test Group: | RT No. 816078 | Vehicle O | % Saline | Test Vansofi 222 Material LOT NO. V20 |
| | • | | • | sterile | (1% w/r. |
| NA | Positive Control | Group NA | _ Vehicle _ | NA | Animal No. 000 |
| | | | | | |

Date Animal Received //16/81

Source Dean Daul Sex O Challenge Date 2/27/8

| | | | | | Tech | Reco | |
|------------------------------|-------------------|-------------------------------------|------------------|-------|-------------|-------------|--------|
| Sensi- tizing Dose No. | Dose ² | Obser- vation Period (Hrs) | Eryth ema | Edema | Cechnic (an | Recorded By | 1981 |
| / | 0.5 | na. | na | na | нн | 44 | 1120 |
| | | 24 | 0 | 0 | 45 | الكا | 1 1/27 |
| | | 48- | - 0 | 0 | 1 7 | 1 1 | 1/18 |
| | 0.5 | NA | NA | NA_ | NON | 100 | 1/28 |
| | | 24 | 0 | 0 | HH | HH | 1/29 |
| | | 48 | 0 | 0 | سبح | سع | 1/30 |
| • | 0.5 | NA | na | NA | Sw | Sw | 1/30 |
| 3 | : | 24 | 0 | 0 | as. | 100 | 1/31 |
| ÷ | | . 48 - : | O . | 1 0 | Co | <u>1 00</u> | 2/1 |
| : , / | 0.5. | NA | NA. | NA | R | 100 | |
| 4 | | . 24 | <u> </u> | 0 | 1 44 | . HH . | 2/3 |
| | 1 | : 48 - | 0 | 0_ | NOR | Co | 44 |
| _ | 0.5 | NA | NA | NA | 1111 | нн | |
| 5 | | 24 | 110 | 0 | 11/10 | 11.78 | 2/5 |
| | 1 ' | 48 | 1,0 | 0_ | <u> </u> | 1 36 | 2-6 |

a - Dosage applied by technician indicated

NA - Not Applicable

| | DERINE S | DIGITLE | ALION STOBI | IN GOINEA | PIGS | - Marie | ACL 277.9 |
|-------------|------------------|-----------|-------------|-------------|----------------------|-----------------------------|-----------|
| \boxtimes | Test Group: | RT No. | 810018 | Vehicle O. | 7% Saline Sterile | Test Vans Material LOT M | VO. Y2010 |
| NA | Positive Control | | | | | Animal No. | |
| Date A | nimal Received | 1/16 | /81 | | | Date Initiated | 1/26/ |
| Source | Dean Day | <u>./</u> | Sex | · | | hallenge Date | 2/27/ |

| | | | • | | Tech | Rec | L |
|------------------------------|-------------------|-------------------------------------|----------|-------|---------|-------------|------------------|
| Sensi- tizing Dose No. | Dose ² | Obser- vation Period (Hrs) | Erythema | Edema | mic lan | Recorded By | Da Te 198/ |
| 6 | 0.5 | na | NA | NA. | Sw | Sw | 2/6 |
| | | 24 | 1.0 | 1.0 | OCAN | 1 740 | 2/7 |
| | | 48. | . 0_ | 1 | 440 | 11/20 | 2/8 |
| 7 | 0.5 | NA | NA | NA | TP | R | 2/9 |
| / | | 24 | 1.0 | 1.0 | NOO | ليكيا | 2/10 |
| | | 48 | 1.0 | 1.0 | Co | Co | 2/11 |
| | 0.5 | NA . | NA | NA | 5G | SG | 2-11 |
| .8 | | 24 | 1.0 | 1.0 | dil | 148 | 2-12 |
| . 0 | | 48 - | 1.0 | 0 | dil | 1 Sw | 2/13 |
| . Q. | 0.5 | : NA | . NA | NA. | · yyo | m | 2/13 |
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| | į | : 48 ¥ | 1.0 | 0 | ŚG | : 56 | 2-15 |
| Challenge Dose | 0.5 | NA | NA | NA. | R | TP | 2/27 |
| DASS | | 24 | 0 | 0 | 140 | 200 | 2/28 |
| WU38 | | 48 | 0 | 0 | M | shot ! | 3/1 |

a - Dosage applied by technician indicated
 NA - Not Applicable



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A Division of Raiston Purina Company

GUINEA PIG MAXIMIZATION STUDY OF VARISOFT 222-90% (LOT NO. V2010315)

SPONSOR: SHEREX CHEMICAL COMPANY

DUBLIN, OH 43017

STUDY NO.

816078

INITIATION:

1/5/81 1/29/81

COMPLETION: REPORTED:

2/24/81

SAMPLE: Varisoft 222-90% (Lot No. V2010315)

ENCLOSED: METHOD, PAGE 2 and 3

SUMMARY, PAGE 4
RAW DATA APPENDIX

SIGNED:

NANCY J ALBRECHT, BA

TECHNICAL SUPERVISOR

GARY W. THOMPSON, BS

HEAD, ACUTE TOXICOLOGY

STUDY DIRECTOR

BY AND FOR RALTECH SCIENTIFIC SERVICES

RAW DATA FOR THIS STUDY IS KEPT ON FILE AT RALTECH SCIENTIFIC SERVICES, MADISON, WISCONSIN.

3301 KINSMAN BLVD. • P.O. BOX 7545 • MADISON, WISCONSIN 53707 • PHONE (608) 241-4471 • TLX 260098 HAZRAL MDS

Guinea Pig Maximization Study
Test Material Varisoft 222-90% (Lot No. V2010315)
Study No. 816078

Sponsor

Sherex Chemical Company P. O. Box 646 Dublin OH 43017

Principal Investigator

Robert L. Harrison

Contractor

Hazleton Raltech, Inc. 3301 Kinsman Boulevard Madison WI 53704

Study Director

Gary W. Thompson, BS

Amendment No. 1 to the Report

Reason

The stated volume of the dose was incorrect and the method of application of the test substance during intradermal injections was not clarified in the "Method" section of the final report.

Change

The Method section on page 2 of the final report, sentence 2, should be corrected to read:

"...one row on each side of the midline as follows: 0.05 ml of prepared Freund's Adjuvant Solution, 0.05 ml of the 5% aqueous test solution, and 0.05 ml of a 5% solution of test material and Freund's Adjuvant Solution."

Gary W. Thompson, BS

Study Director, Acute Toxicology

6-4-82

Date

by and for Hazleton Raltech, Inc.

/dka



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RT LAB NUMBER 816078
GUINEA PIG MAXIMIZATION

PAGE 2

Test Material: Varisoft 222-90% (Lot No. V2010315)

Test Animal: Young adult male guinea pigs were procured, maintained individually in stainless steel cages in temperature and humidity controlled rooms, provided continuous access to Purina Guinea Pig Chow and water and held for a conditioning period of at least 7 days.

Test System: Ten male guinea pigs weighing between 425 and 494 grams were chosen at random and used for this study. The animals were individually housed and identified by animal number and ear tag.

Preparation of Test Material: For the intradermal injections the Freund's Complete Adjuvant Solution was prepared by adding 5.0 mL of sterile water: for injection in 1.0 mL increments to 5.0 mL of Freund's Adjuvant.

The 5% solution of test material in sterile water was prepared by taking 0.5 gram of Varisoft 222-90% (Lot No. V2010315) and adding sterile water for injection to a total volume of 10.0 mL.

The 5% solution of test material in Freund's Adjuvant was prepared by placing 0.5 g of Varisoft 222-90% (Lot No. V2010315) into a 30-mL beaker and adding sterile water to a Q.S. volume of 5.0 mL. To this, 5.0 mL of Freund's Adjuvant was added in 1.0 mL increments while stirring.

For the topical induction the Varisoft 222-90% (Lot No. V2010315) was administered at a concentration of 25% w/v in sterile saline. For the challenge procedures, the test material was administered at a 1.0% w/v concentration in sterile saline.

Method: A 4.0 x 6.0 cm area was clipped along the midline over the shoulder region. Two rows of three-deep intradermal injections (total of 6 injections) were made within the boundaries of a 2.0 x 4.0 cm area, one row on each side of the midline as follows: 0.1 mL of the prepared Freund's Adjuvant Solution, 0.1 mL of a 5% aqueous test solution, and 0.1 mL of a 5% solution of test material and Freund's Adjuvant Solution.

One week after the injections, the same area was clipped and closely shaved with an electric razor. A 2.0 x 4.0 cm patch of Whatman No. 3 filter paper was saturated with a 25% w/v solution of Varisoft 222-90% (Lot No. V2010315) and sterile 0.9% saline, placed over the injection sites, then covered with an overlapping of Blenderm tape and secured by an overwrap of Elastoplast tape. The dressing remained in place for 48 hours.



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A Division of Relation Purms Company

RT LAB NUMBER 816078
GUINEA PIG MAXIMIZATION

PAGE 3

Two weeks after topical induction the animals received a challenge dose. The hair was removed from a $5.0 \times 5.0 \text{ cm}$ area on the flank by clipping and shaving as before. A 1.0% w/v solution of the test material in sterile 0.9% saline was applied on a $2.0 \times 2.0 \text{ cm}$ piece of filter paper in the same fashion as for topical induction. The patch was sealed to the flank for 2% hours under a 4.0 cm strip of Blenderm tape. Complete occlusion was made by an overwrap with Elastoplast tape wound around the trunk.

Observations: Twenty-four hours following patch removal the test sites were examined for erythema and edema. The sites were examined again at 48 hours after patch removal to detect weak, slowly developing reactions. The test sites were shaved 3 hours prior to the 24-hour reading. The reactions were scored according to the following 4-point scale:

- 0 = no reaction
- l = scattered mild redness
- 2 = moderate and diffuse redness
- 3 = intense redness and swelling

The important statistic in maximization testing is the frequency of sensitization, not the intensity.



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RT LAB NUMBER 816078
GUINEA PIG MAXIMIZATION

PAGE 4

Test Animal: Albino guinea pigs

Source: Dean Dahl, Luxemburg, Wisconsin

Date Animals Received: 12/23/80

Test Material: Varisoft 222-90% (Lot No. V2010315)

Date Test Started: 1/5/81 Date Test Completed: 1/29/81

| Animal | | Challenge Dose Reactions | | | |
|----------|------------|--------------------------|----------|--|--|
| Number | <u>Sex</u> | 24 Hours | 48 Hours | | |
| 64000712 | M | 0 | 0 | | |
| 64000713 | M | 0 | 0 | | |
| 64000714 | M | Ö | 0 | | |
| 64000716 | M | Ö | <u> </u> | | |
| 64000717 | M | 0 | 0 | | |
| 64000718 | M | 0 | 0 | | |
| 64000719 | M | 0 | 0 | | |
| 64000721 | M | 0 | 0 | | |
| 64000722 | . <u></u> | 0 | 0 | | |
| 64000723 | M | 0 | 0 | | |

General Behavior and Appearance:

All of the guinea pigs used in this study appeared normal throughout the study period. Normal body weight gains were recorded for all animals during the course of the study.

Skin Reactions to Varisoft 222-90% (Lot No. V2010315):
None of the ten guinea pigs exhibited a reaction to the challenge dose at either the 24 or 48 hour observations.

Conslusion:

Based upon the results obtained, the test material, Varisoft 222-90% (Lot No. V2010315), is not considered a skin sensitizer.

References

Magnusson, B., MD, and A. Kligman, PhD, MD, Allergic Contact Dermatitis in the Guinea Pig, Charles C. Thomas, pub., 1970, pp. 113-117.

Dermal Sensitization In Guines Pigs - Body Weights

| \boxtimes | Test Group RT No. 816078 Vehicle NA Te | est Compound Varisoft 222-9 |
|-------------|--|-----------------------------|
| มก | Positive Control Group NA Vehicle NA | NOT NO. V20/03/5 |

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| 459 | 485 | 523 | 533 | SOF | 511 | 530 | 517 | IP | 1/261 |
| 461 | 461 | 542 | 538 | 526 | 515 | 522 | 534 | | |
| 514 | 544 | 627 | 638 | 585 | 558 | 625 | 626 | PS | Freker |
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| | · | - | | | | | | | |

| | | Animal Number | 丁 🤼 | |
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| 548 | 532 | Scale Used: K-Tron 4809 | PSW | |
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| | | Scale Used: | J. 30 | 1/26/3/ |
| | | Scale Used: | | |

NA - Not Applicable

GUINEA PIG MAXIMIZATION TEST

and the second section of the section of

| Test Compo | und Vario | SOST 222-90% | 7 | RT No. | 816078 |
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| pH Result | | OT NO. VZ 01031; | 5 | | NN |
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| 0723 | ♂ . | 0 | | 0 | |
| Technician | | HH | | np | |
| Recorded By | | HH | | M | |
| Date | = Townsel | /z8/8/ | | 1/29/81 | |
| | | | | 1-1/81 | |

Scoring Code: 0 = Normal, No Reaction

1 = Scattered Mild Redness

2 - Moderate and Diffuse Redness

3 = Intense Redness and Swelling

REVIEWED BY: NOT DATE: 1/29/87

Test Group RT No. 81/2078 Vehicle NTO Test Compound Varisot 222-90

Positive Control Group NA Vehicle NTO Room No. 1/21 B **

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N - No Visible Abnormalities

*Test animals No - Not applicable moved to room 3 on 1/15/81 NOP.

| | Test Group RT No | | ···· | | Varisof 222 Lot No. V2010 161 G-X | ^ ⊃ ! |
|------|------------------|---------------|------|-------------|---|--------------|
| | | Animal Number | | | - | |
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N - No Visible Abnormalities

NA - Not Applicable

*Test animals moved To room 3 on 1/15181 NOR

Test Group RT No. 8/6078 Vehicle NA Test Compound Varisoft 222-90

NA Positive Control Group NA Vehicle NA Room No. 16/8*

| | Animal Number | | | | | | | | | | | |
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N - No Visible Abnormalities

NA - Not Applicable

* Test animals moved to

| X | Test Group RT No. 816078 Vehicle | NA Test Compound Varisof+ 222- |
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| MA | Positive Control Group NA Ve | chicle NA Room No. 1618 |

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N - No Visible Abnormalities

NA - Not Applicable

*Test animals moved to room 3 on 11881 NOO

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Guinea Pig Maximization Study Test Material Varisoft 222-90% (Lot No. V2010315) Study No. 816078

Sponsor

Sherex Chemical Company P. O. Box 646 Dublin OH 43017

Principal Investigator

Robert L. Harrison

Contractor

Hazleton Raltech, Inc. 3301 Kinsman Boulevard Madison WI 53704

Study Director

Gary W. Thompson, BS

Amendment No. 1 to the Report

Reason

The stated volume of the dose was incorrect and the method of application of the test substance during intradermal injections was not clarified in the "Method" section of the final report.

Change

The Method section on page 2 of the final report, sentence 2, should be corrected to read:

"...one row on each side of the midline as follows: 0.05 ml of prepared Freund's Adjuvant Solution, 0.05 ml of the 5% aqueous test solution, and 0.05 ml of a 5% solution of test material and Freund's Adjuvant Solution."

Gary W. Thompson, BS

Study Director, Acute Toxicology

6-4-82 Date

by and for Hazleton Raltech, Inc.

/dka



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A Division of Raiston Purine Company

RT LAB NUMBER 816078
GUINEA PIG MAXIMIZATION

PAGE 2

Test Material: Varisoft 222-90% (Lot No. V2010315)

Test Animal: Young adult male guinea pigs were procured, maintained individually in stainless steel cages in temperature and humidity controlled rooms, provided continuous access to Purina Guinea Pig Chow and water and held for a conditioning period of at least 7 days.

Test System: Ten male guinea pigs weighing between 425 and 494 grams were chosen at random and used for this study. The animals were individually housed and identified by animal number and ear tag.

Preparation of Test Material: For the intradermal injections the Freund's Complete Adjuvant Solution was prepared by adding 5.0 mL of sterile water: for injection in 1.0 mL increments to 5.0 mL of Freund's Adjuvant.

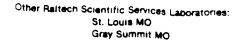
The 5% solution of test material in sterile water was prepared by taking 0.5 gram of Varisoft 222-90% (Lot No. V2010315) and adding sterile water for injection to a total volume of 10.0 mL.

The 5% solution of test material in Freund's Adjuvant was prepared by placing 0.5 g of Varisoft 222-90% (Lot No. V2010315) into a 30-mL beaker and adding sterile water to a Q.S. volume of 5.0 mL. To this, 5.0 mL of Freund's Adjuvant was added in 1.0 mL increments while stirring.

For the topical induction the Varisoft 222-90% (Lot No. V2010315) was administered at a concentration of 25% w/v in sterile saline. For the challenge procedures, the test material was administered at a 1.0% w/v concentration in sterile saline.

Method: A 4.0 x 6.0 cm area was clipped along the midline over the shoulder region. Two rows of three-deep intradermal injections (total of 6 injections) were made within the boundaries of a 2.0 x 4.0 cm area, one row on each side of the midline as follows: 0.1 mL of the prepared Freund's Adjuvant Solution, 0.1 mL of a 5% aqueous test solution, and 0.1 mL of a 5% solution of test material and Freund's Adjuvant Solution.

One week after the injections, the same area was clipped and closely shaved with an electric razor. A 2.0 x 4.0 cm patch of Whatman No. 3 filter paper was saturated with a 25% w/v solution of Varisoft 222-90% (Lot No. V2010315) and sterile 0.9% saline, placed over the injection sites, then covered with an overlapping of Blenderm tape and secured by an overwrap of Elastoplast tape. The dressing remained in place for 48 hours.





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RT LAB NUMBER 816078
GUINEA PIG MAXIMIZATION

PAGE 3

Two weeks after topical induction the animals received a challenge dose. The hair was removed from a 5.0×5.0 cm area on the flank by clipping and shaving as before. A 1.02 w/v solution of the test material in sterile 0.9% saline was applied on a 2.0×2.0 cm piece of filter paper in the same fashion as for topical induction. The patch was sealed to the flank for 24 hours under a 4.0 cm strip of Blenderm tape. Complete occlusion was made by an overwrap with Elastoplast tape wound around the trunk.

Observations: Twenty-four hours following patch removal the test sites were examined for erythema and edema. The sites were examined again at 48 hours after patch removal to detect weak, slowly developing reactions. The test sites were shaved 3 hours prior to the 24-hour reading. The reactions were scored according to the following 4-point scale:

0 = no reaction

1 = scattered mild redness

2 = moderate and diffuse redness

3 = intense redness and swelling

The important statistic in maximization testing is the frequency of sensitization, not the intensity.



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RT LAB NUMBER 816078
GUINEA PIG MAXIMIZATION

PAGE 4

Test Animal: Albino guinea pigs

Source: Dean Dahl, Luxemburg, Wisconsin

Date Animals Received: 12/23/80

Test Material: Varisoft 222-90% (Lot No. V2010315)

Date Test Started: 1/5/81

Date Test Completed: 1/29/81

| Animal | | Challenge Dose Reactions | | | | |
|----------|------------|--------------------------|----------|--|--|--|
| Number | <u>Sex</u> | 24 Hours | 48 Hours | | | |
| 64000712 | М | 0 | 0 | | | |
| 64000713 | M | 0 | 0 | | | |
| 64000714 | M | Ō | ő | | | |
| 64000716 | M | 0 | 0 | | | |
| 64000717 | M | 0 | 0 | | | |
| 64000718 | М | 0 | 0 | | | |
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| 64000721 | M | 0 | 0 | | | |
| 64000722 | M | o o | 0 | | | |
| 64000723 | M | Ö | 0 | | | |

General Behavior and Appearance:

All of the guinea pigs used in this study appeared normal throughout the study period. Normal body weight gains were recorded for all animals during the course of the study.

Skin Reactions to Varisoft 222-90% (Lot No. V2010315):

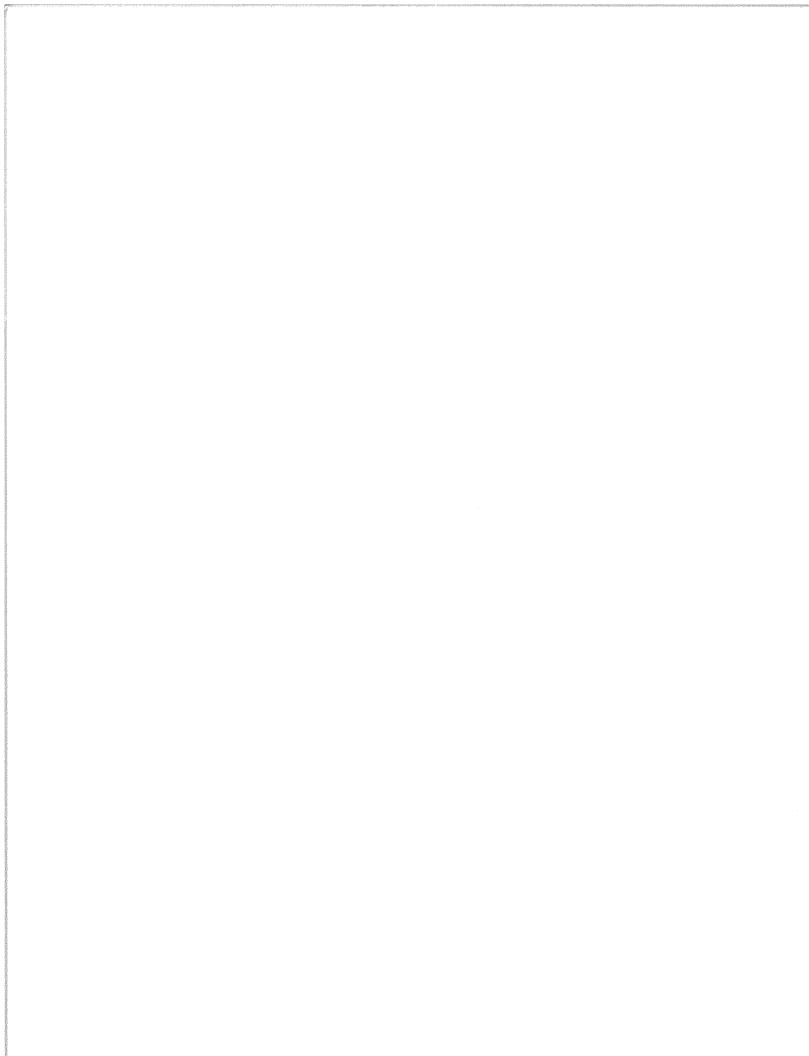
None of the ten guinea pigs exhibited a reaction to the challenge dose at either the 24 or 48 hour observations.

Conslusion: _ -

Based upon the results obtained, the test material, Varisoft 222-90% (Lot No. V2010315), is not considered a skin sensitizer.

Reference:

Magnusson, B., MD, and A. Kligman, PhD, MD, Allergic Contact Dermatitis in the Guinea Pig, Charles C. Thomas, pub., 1970, pp. 113-117.



Dermal Sensitization In Guines Pigs - Body Weights

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NA - Not Applicable

GUINEA PIG MAXIMIZATION TEST

| | Test Compou | and Varis | oft 222-90; TNO. VZ 01031 | The second secon | RT No. | 816078 |
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Scoring Code: 0 = Normal, No Reaction

1 = Scattered Mild Redness

2 = Moderate and Diffuse Redness

3 = Intense Redness and Swelling

REVIEWED BY: NA DATE: 1/29.

Test Group RT No. 8110018 Vehicle NO Test Compound Varisoft 2722-90

NO Positive Control Group NA Vehicle NO Room No. 101 B

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N - No Visible Abnormalities

*Test animals #- Not applicable moved to room 3 on 1/15/81 NOTO.

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N - No Visible Abnormalities

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*Test animals moved To room 3 on 1/15/8/ NOO

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N - No Visible Abnormalities

NA - Not Applicable

* Test animals moved to

| Name of the last o | Test Grow | ip RT | No. 3 | 816078 | Vehicle | NA. | Test | Compound | Varis | St. 2. | ZZ-% |
|--|-----------|--------|--------|--------|---|---------|----------------|----------------|-------|--------|------|
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W - No Visible Abnormalities

NA - Not Applicable

Frest animals moved to



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REPORT

P.L. HARRISON SHEREK CHEMICAL COMPANY, INC. P.O. BOX 646 DUBLIN, OH 43017

RT LAB NO. 816079

ENTERED 11/13/80

REPORTED 04/02/81

VARISOFT 222-90%: LOT #V2010225

PURCHASE ORDER NUMBER 020-48946 £ 53

ENCLOSED:

GUINEA PIG SENSITIZATION - METHOD, SUMMARY

RAW DATA ATTACHED

SIGNED:

GARY W. THOMPSON, BS HEAD, ACUTE TOXICOLOGY

BY AND FOR RALTECH SCIENTIFIC SERVICES, INC.

3301 KINSMAN BLVD. • P.O. BOX 7545 • MADISON, WISCONSIN 53707 • PHONE (608) 241-4471 • TLX 260098 HAZRAL MDS

Guinea Pig Sensitization (Closed Patch Technique)
Test Material Varisoft 222-90% (Lot No. V20100225)
Study No. 816079

Sponsor

Sherex Chemical Company P. O. Box 646 Dublin OH 43017

Principal Investigator

Robert L. Harrison

Contractor

Hazleton Raltech, Inc. 3301 Kinsman Boulevard Madison WI 53704

Study Director

Gary W. Thompson, BS

Amendment No. 1 to the Report

Reason

The "High" score for animal 64100019 is incorrectly listed as (1).

Change

The Challenge Phase erythema high score for animal number 64100019 should be changed to (0).

Gary W. Thompson, BS

Study Director, Acute Toxicology

by and for Hazleton Raltech, Inc.

/dka





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RT LAB NUMBER 816079

PAGE 2

VARISOFT 222-90%: LOT #V2010225

SKIN SENSITIZATION

TEST ANIMAL: FOURTEEN MALE ALBINO GUINEA PIGS OF THE HARTLEY STRAIN, WEIGHING BETWEEN 444 AND 520 GRAMS, WERE USED FOR THIS STUDY. THE ANIMATION WERE INDIVIDUALLY HOUSED IN SCREEN BOTTOM CAGES IN A TEMPERATURE AND HUMIDITY CONTROLLED ROOM, PROVIDED CONTINUOUS ACCESS TO COMMERCIAL LABORATORY FEED AND WATER AND HELD FOR AN ACCLIMATION PERIOD OF AT LEAST SEDAYS. EACH ANIMAL WAS IDENTIFIED BY AN ANIMAL NUMBER AND CORRESPONDING EAP TAG. THE ACCLIMATED ANIMALS WERE DIVIDED INTO TWO GROUPS CONSISTING OF A NAIVE UNTREATED CONTROL GROUP OF FOUR GUINEA PIGS AND A TREATED GROUP TEN GUINEA PIGS.

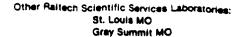
PREPARATION OF TEST MATERIAL: TO PREPARE A 1% WEIGHT TO VOLUME MIXTURE,
1.00 G OF THE TEST MATERIAL WAS WEIGHED INTO AN ERLENHEYER FLASK. STERI
0.9% SALINE WAS ADDED TO MAKE A TOTAL VOLUME OF 100 ML.

THE DOSAGE LEVEL WAS SELECTED BASED UPON RESULTS OBTAINED FROM A RANGE FINDING STUDY UTILIZING CONCENTRATIONS OF 1.0, 10.0, 25.0, 50.0, 75.0 AN 100% W/V MIXTURES OF TEST MATERIAL IN STERILE 0.9% SALINE.

TREATMENT: PRIOR TO EACH APPLICATION THE HAIR WAS REMOVED FROM THE BACK OF EACH ANIMAL WITH ELECTRIC CLIPPERS. THE TEST MATERIAL WAS APPLIED TO ON AREA ON EACH ANIMAL BY PLACING 0.5 ML OF THE 1% W/V MIXTURE OF TEST MATERIAL ON A WEBRIL PAD (7/8 INCH X 1 INCH) AND PLACING THE PAD ON THE TEST SITE ALONG THE MIDLINE OF THE BACK. THE PATCH WAS COVERED WITH RUBBER DAM AND SECURED WITH AN OVERWRAP OF ELASTOPLAST TAPE. THE DRESSI REMAINED IN PLACE FOR A PERIOD OF SIX HOURS AT WHICH TIME IT WAS REMOVED

THE TEST GROUP ANIMALS RECEIVED THREE APPLICATIONS PER WEEK FOR THREE WE FOR A TOTAL OF NINE APPLICATIONS.

TWO WEEKS FOLLOWING THE ADMINISTRATION OF THE NINTH SENSITIZING DOSE, A CHALLENGE DOSE OF 0.5 ML OF A 1% WEIGHT TO VOLUME MIXTURE OF THE TEST MATERIAL IN STERILE 0.9% SALINE WAS ADMINISTERED TO THE TEST GROUP IN THE SAME MANNER AS DURING THE SENSITIZING PHASE OF THE STUDY. AT THIS TIME, A GROUP OF FOUR NAIVE (PREVIOUSLY UNTREATED) CONTROL ANIMALS WAS ALSO TREATED WITH THE CHALLENGE DOSE.





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BI LAB NUMBER 816079

PAGE 3

VARISCRT 222-90%: LOT #V2010225

SKIN SENSITIZATION (CONTINUED)

OBSERVATIONS: THE APPLICATION SITES WERE READ AND SCORED FOR ERYTHEMA AND EDEMA AT 24 AND 48 HOURS FOLLOWING EACH APPLICATION ACCORDING TO THE DRITECHNIQUE.* REACTIONS TO THE CHALLENGE DOSE WERE READ AND SCORED AT 24 48 HOURS AS WAS DONE FOLLOWING THE SENSITIZING APPLICATIONS. THE ANIMAL WERE OBSERVED FOR GENERAL BEHAVIOR AND APPEARANCE ONCE DAILY DURING THE FINTIRE STUDY PERIOD. BODY WEIGHTS WERE TAKEN AT STUDY INITIATION AND ATWEEKLY INTERVALS DURING THE STUDY.

PATHOLOGY: AT STUDY TEPMINATION ALL ANIMALS WERE EUTHANATIZED AND DISCARD

SENSITIZATION RATINGS

SENSITIZATION RATE

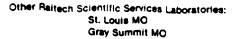
10 - 30%

40 - 70%

80 - 100%

CLASSIFICATION
WEAK SKIN SENSITIZER
MODERATE SKIN SENSITIZER
STRONG SKIN SENSITIZER

*DRAILE, J.H., 1965, APPRAISAL OF THE SAFETY OF CHEMICALS IN FOODS, DRUGS AND COSMETICS - DERMAL TOXICITY. ASSOCIATION OF FOOD AND DRUG OFFICIALS OF THE U.S., TOPEKA, KANSAS, PP. 49-51.





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RI LAE NUMBER 816079

PAGE 4

VARISOFT 222-90%: LOT #V2010225

SKIN SENSITIZATION (CONTINUED)

TEST ANIMAL: GUINEA FIGS

SOURCE: DEAN DAUL, LUMEMBURG, WI DATE ANIMALS RECEIVED: 1/16/81

DATE TEST STARTED: 1/26/81 DATE TEST COMPLETED: 3/1/81

SUMMARY OF SKIN REACTIONS**

| | CHALLENGE PHASE | | | | | | | | |
|----------|-----------------|-----------|--------|--------------|--------------------|----------|--------|------|--|
| | N | INE APPI | .ICATI | ONS | SINGLE APPLICATION | | | | |
| | | (0.5 | ML) | | | (0.5 | ML) | | |
| ANIMAL | ERY | THEMA | Ε | DEMA | ERY | THEMA | EDEMA | | |
| NUMBER | AVE. | (HIGH) | AVE. | (HIGH) | AVE. | (HIGH) | AVE. | (HIG | |
| 64100016 | 0.3 | (1) | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | |
| 64100017 | 0.3 | (1) | 0.1 | (1) | 0.0 | (0) | 0.0 | (0) | |
| 64100019 | 0.1 | (1) | 0.1 | (1) | 0.0 | (0) | 0.0 | (0) | |
| 64100019 | 0.1 | (1) | 0.1 | (1) | 0.0 | (1) | 0.6 | (0) | |
| 64100020 | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | |
| 64100021 | 0.5 | (1) | 0.1 | (1) | 0.0 | (0) | 0.0 | (0) | |
| 64100022 | 0.1 | (1) | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | |
| 64100023 | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | 0.0 | (0) | |
| 64100024 | 0.6 | (2) | 0.3 | (1) | 0.0 | (0) | 0.0 | (0) | |
| 64100025 | 0.6 | (2) | 0.2 | (1) | 0.0 | (0) | 0.0 | (0) | |
| NATUR | (HNTRFATE | 'D) CONTR | | (CHATTENCE D | OCF - VID | TCOF# 22 | 2-007. | | |

TEST GROUP: VARISOFT 222-90% LOT NO. V2010225, 1% W/V

| MAIVE | (UNTREATED) | CONTROL: | (CHALLENGE | DOSE - | · VARISOFT | 222-90%: |
|-------|-------------|----------|------------|--------|------------|----------|
| | | | | | | |

| | | | | LOT NO. V | 2010225, 1% | W/V) | | |
|----------|---|---|---|-----------|-------------|------|-----|-----|
| 64100026 | - | - | - | - | 0.0 | (0) | 0.0 | (0) |
| 64100027 | - | - | - | - | 0.0 | (0) | 0.0 | (0) |
| 64100028 | - | - | _ | - | 0.0 | (0) | 0.0 | (0) |
| 64100029 | - | - | - | - | 0.0 | (O) | 0.0 | (0) |

**THE AVERAGE ERYTHEMA AND EDEMA VALUE IS THE MEAN SCORE FOR THE 18 OBSERV TIONS (SENSITIZING TREATMENT) OR TWO OBSERVATIONS (CHALLENGE TREATMENT) OF THE APPLICATION SITE FOR EACH ANIMAL. THE HIGH READING IS THE HIGHES SCORE RECORDED FOR THE RESPECTIVE ANIMAL DURING THAT PHASE OF THE STUDY.



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A Division of Raiston Purine Company

RT LAS NUMBER 816079

VARISHIT 122-90%: LOT #V2010225

PAGE 5

SKIN SENSITIZATION (CONTINUED)
RESULTS:

GENERAL BEHAVIOR AND APPEARANCE: ALL OF THE GUINEA PIGS USED IN THIS STUD APPEARED NORMAL TEROUGHOUT THE STUDY PERIOD. NORMAL BODY WEIGHT GAINS WERE RECORDED FOR ALL ANIMALS DURING THE COURSE OF THE STUDY.

TEST COMPOUND (VARISOFT 222-90% LOT NO. V2010225, 1% W/V): EIGHT OF THE ANIMALS NERS OBSERVED WITH SLIGHT TO MODERATE ERYTHEMA REACTIONS DURING THE SENSITIZING PHASE OF THE STUDY. SLIGHT EDEMA REACTIONS WERE EXHIBIT BY SIX ANIMALS FOLLOWING THE SENSITIZING APPLICATIONS. TWO ANIMALS (NOS. 64100020 AND 64100023) DID NOT EXHIBIT ANY ERYTHEMA REACTION AND FOUR ANIMALS (NOS. 64100016, 64100020, 64100022 AND 64100023) DID NOT EXHIBIT ANY EDEMA REACTIONS DURING THE SENSITIZING PHASE OF THE STUDY.

NONE OF THE ANIMALS IN THE TEST OR NAIVE CONTROL GROUP EXHIBITED EITHER AN ERITHEMA OR EDEMA RESPONSE TO THE TEST MATERIAL FOLLOWING THE CHALLEN APPLICATION WITH 0.5 KL OF A 1.0% W/V HIXTURE OF TEST MATERIAL IN STERIL 0.9% EALINE.

CONCLUSION: THIS TEST MATERIAL IS NOT CONSIDERED A SKIN SENSITIZER IN GUINEA PIGS BY THE CLOSED PATCH TECHNIQUE.

Dermal Sensitization In Guinea Pigs - Body Weights

Test Group RT No. 810079 Vehicle 0.9% Saline Test Compound 810079

Sterile

Positive Control Group NA Vehicle NA

| | | | Animal | Number | | | | 1 | |
|--------|--------|--------|--------|--------|------|--------|-------|-----------------|------|
| 10410- | 10410- | 60410- | 6410- | 6410 | 6410 | 60410- | 6410- | | |
| 0016 | 7100 | 8100 | 0019 | 0020 | 0021 | 0022 | 0023 | Tech- nician | Dat. |
| 444 | 447 | 467 | 473 | 501 | 444 | 505 | 485 | NDP Sw | 1/26 |
| 508 | 485 | 506 | 533 | 504 | 498 | 576 | 547 | MH | 2/ |
| 557 | 522 | 556 | 582 | 551 | 550 | 635 | 614 | KUN | 2/9 |
| 6.39 | 281 | 610 | 650 | 558 | 621 | 691 | 684 | SW | 2/16 |
| 718 | 761 | 675 | 702 | 608 | 710 | 758 | 771 | 25 | 2/23 |
| 20 | | | | | | | | | |

| | | Anima | al Number | | |
|----------------|------|-------------|--------------|-----------------|------------|
| 10410- 0024 | 0025 | | • | Tech- nician | Date / 98/ |
| 520 | 489 | Scale Used: | K-Tron 4809 | 100 500 | 1/2/ |
| 6/2 | 549 | Scale Used: | X-Tron 4809 | | |
| 7010 | 623 | Scale Used: | K-7 ROW 4507 | `,,,\\\ | 2/7 |
| 740 | 681 | Scale Used: | K-Tron 4809 | SW | 2/16 |
| 851 | 769 | Scale Used: | Penn 37.28 | NJA | 2/23 |
| -VR | Na | Scale Used: | 21/ | NA | 4 |

Dermal Sensitization In Guinea Pigs - Body Weights

| NA | Test Group RT No. 810079 | Vehicle 09% Saling Test | Varisoft 222-C Compound LOT NO. V201022 |
|----|--------------------------|-------------------------|--|
| | Naive Untreated Control | | (190 WIr) |

| | | | Animal | Number | | | | |
|------|-----|------|--------|--------|---|--|-----------------|--------------|
| | 1 | 0028 | | | · | | Tech- nician | Date 1981 |
| 484. | 497 | 474 | 486 | | | | NJA Sw | 1/26 |
| 553 | 588 | 560 | 562 | | | | 1 | 2/2 |
| 624 | 642 | 622 | 637 | | | | SW. | 219 |
| 692 | 70a | 691 | 733 | | _ | | لستح | 2/16 |
| 768 | 762 | 751 | 808 | | | | NON | 2/23 |
| 4 | | | | | | | 1 | J |

| | Anim | al Number | | |
|--|-------------|-------------|-----------------|--------------|
| | | | Tech- nician | Date /98/ |
| | Scale Used: | K-Tron 4809 | NDASW | 1/26 |
| | Scale Used: | K-Tron 4809 | 1 HH | 2/2 |
| | Scale Used: | K-TRON 4809 | OCU | 2/9 |
| | Scale Used: | K-Tron 4809 | Sw | 2/16 |
| | Scale Used: | Penn 3728 | NO | 3/23 |
| | Scale Used: | NA- | | 7 |

Naive Untreated Control RT No. 8110079 Vehicle 0.990 Saling . Sterile

| Date Animal Received \\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\ | 181 | | ·. |
|---|-----|----------------|--------|
| Source Dean Daul | Sex | Challenge Date | 2/27/8 |

| | | | | | Tech | Rec | |
|------------|-------------------|-------------------------------------|----------|--------|------------|-------------|-----------|
| Animal No. | Dose ² | Obser- vation Period (Hrs) | Erythema | Edema | Technician | Recorded By | Date 1981 |
| 0026 | 0.5 | NA | AX. | NA | R | R | 2/27 |
| | | 24 48 | 0 | 0 | 20 | 1 17 | |
| 6410- | 0.5 | NA | NA. | NA. | R | TP | 2/0 |
| 0027 | ļ | 24 48 | 0 | 0 | JP Mp | JP PAP | 3/1 |
| 6410- | 0.5 | NA NA | NA NA | · NA | JR | R | 3/27 |
| 0028 | | 24 48 | | 0 | 790 | R | 3/1 |
| 6410- | 0.5 | NA | | | R | R | 2/07 |
| 0029 | | 24 48 | 0 | 0 C | مهر ا | 17 | 748 |
| | | - NA | NA | NA | | | |
| | | 24 48 | | | | | |

a - Dosage applied by technician indicated
 NA - Not Applicable

| Tes | t Group: | RT No. 816 | Vehic | steri | line Mater 10 Anis | Varisof rial LOTNO.V (176 410- val No. | 7 20 N |
|------------------------------|------------------------|-------------------------------------|------------|---------|--------------------------|--|--------|
| | _ | 1/16/81 aul sex | | | | Initiated // | |
| | 1 | 0 | | | Technic Le | Date | |
| Sensi- tizing Dose No. | Dose ² (m1) | Obser- vation Period (Hrs) | Erythema | Edema | Len | 1981 | |
| Ι. | 0.5 | NA 24 48 | NA C | NA O | NH TYP TH | HH 1310 SW 1/27 HH V28 | |
| 2 | 0.5 | NA 24 48 | NA O | NA O | НН | HH 1/28 HH 1/29 Sw 1/30 | 7 |
| 3 | 0.5 | NA 24 | NA /. O | NA O | mg. | mp 1/30 | |
| _ | - I | 4.8 | | 1 6 | 1 717 | 77 2/2 | |

NA

1.0

AK

NA.

NA 24 48

NA

24 48

0.5

0.5

a - Dosage applied by technician indicated
 NA - Not Applicable

| | \boxtimes | Test Group: | RT No. 816 | 079 Vehic | 1.0,9% Sal | line Test le Materia | Variso 120 <u>140.</u> (1 7 0 | 11 222 <u>12010</u> W/V |
|---|-----------------------------|-------------------|----------------------------|-----------|------------|-------------------------|--|-------------------------------|
| | NA | Positive Contro | ol Group | Vehi | cle NA | Aniwal | 0- No. 00 | 125 |
| | | Dean D | | | | Date Ini | | |
| | | • | | | | Rech | F | 7 |
| - | Sensi- tizing Dose No | Dose ² | Obser- vation Period | Erythema | Edema | orded By | Date | |

| Sensi- tizing Dose No. | Dose ² (ml) | Obser- vation Period (Hrs) | Erythema | Edema | <u>11 C (8)1</u> | orded By | 1981 |
|------------------------------|------------------------|-------------------------------------|----------|-------|------------------|---------------|------|
| , . | 0.5 | NA | NA | NA | Sw | Sw | 26 |
| 6 | | 24 | 2.0 | 1.0 | 1XX | 1 20 | 2/7 |
| | | 48 | 4.00 | O | 1 10 | 11000 | 3/8 |
| 1 7 | 0.5 | NA | NA | NA | R | R | 2/9 |
| | | 24 | 1.0 | 0 | ALT PA | Sw | 2/10 |
| | | 48 | 1.0 | 0 | Go | Bo | 2/11 |
| | 0.5 | · NA | NA | NA | こり | 1021 | या |
| 1 X | | -24 | 1-0 | 0_ | m | 1 26 | 3-12 |
| 0 | | 48 | 1.0 | 0 | dh | لىك ا | 3/13 |
| a | 0.5 | NA | NA | NA. | Sw | Sw | ಎ/,3 |
| 1 | | 24 | 0 | | HH | . HH | 2/14 |
| | | 48 | 0 | | \$6 | <u>طکن پُ</u> | 2-15 |
| Challenge | 0.5 | NA | NA | N.A. | R | 17 | 2/27 |
| Dose | | 24 | 0 | 0 | JP | 177 | 3/20 |
| 50-0 | ļ | 48 | 0 | 0 | 140 | ma | 3/1 |

a - Dosage applied by technician indicated
 NA - Not Applicable

D = desquamation 618181 NJA

| DERMAL S | SENSTITZATION ST | GBI IN GUINEA | PIGS | 16 |
|----------------------|------------------|---------------|--|---|
| Test Group: | RT No. 81607 | 9 Vehicle0,9 | 1% Soline Mati | t Varisof1 222- erial LOTNO, V20107. (17 w/v) |
| NA Positive Control | | | NA An | #10- imal No. 0024' |
| Date Animal Received | | | | Initiated //26/8/ |
| Source Dean Da | <u>u</u> /Sex | <u>d'</u> | Challe | enge Date <u>2/27/8</u> |
| | | | · Ee | Re |
| | | | \\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\ | 16 15 1 |

| | | | | | Tech | Reco | 2 |
|------------------------------|------------------------|-------------------------------------|----------|----------|-------------|---------------|------|
| Sensi- tizing Dose No. | Dose ² (mi) | Obser- vation Period (Hrs) | Erythema | Edema | Technic Lan | Recorded by | 1981 |
| , • | 0.5 | NA | NA | NA | HH | HH | 1/26 |
| 1 | | 24 48 | -8 | 0 | HH | MH | 1/27 |
| | 100 | 40 | <u> </u> | 1 | <u> </u> | <u>' 7777</u> | |
| | 0.5 | NA | NA NA | NA | HH | HH | 128 |
| 2 | | 24 | 0 | | 4H Sw | 17H | 1120 |
| | | 48 | 0 | - | 300 | Sw | OE/I |
| _ | 0.5 | · NA | NA . | NA | 35 | m | 1/30 |
| 3 | | 24 | 0 | | P | IP | 1/31 |
|) | | 48 - | 0 | <u> </u> | J. | 177 | 21, |
| 4 <i>l</i> . | 0.5 | NA | NA. | NA | R | 177 | 2/2 |
| 7 | | 24 | 0 | 0 | 144 | · HH | |
| | | 48 | 0 | 0 | NID | Co | 2/4 |
| 5 | 0.5 | NA | NA | NA. | НН | 447 | 2/4 |
| | | 24 | 0 | 0 | NOR | NUN | 215 |
| 1 |] | 48 | 0 | 1 | 56 | 156 | 2-6 |

a - Dosage applied by technician indicated
 NA - Not Applicable

| DERMAL S | PHOTITI | ATTON STOUT | IN GOTHER | PIGS | - . \ | lanicali 227 |
|----------------------|------------|-------------|-----------|-----------|--------------------|---|
| Test Group: | RT No. | 8110079 | Vehicle O | 9% Saline | Test V Material | orisoft 222- 10 <u>110.120107</u> (1 % w/v) |
| NA Positive Control | | | Vehicle | NA | Animal | No. 0024 |
| Date Animal Received | 1/16 | 181 | · —— | 1 | Date Init | iated 1/26/8/ |
| Source Dean Da | <u>u /</u> | _ Sex | | . CI | nallenge | Date 2/27/8 |

| | | | | | Tech | Reco | D. |
|------------------------------|---------------------------|-------------------------------------|----------|-------|--------------------|-------------|-------|
| Sensi- tizing Dose No. | Dose ² (ml) | Obser- vation Period (Hrs) | Erythema | Edema | <u>Technic Lan</u> | Recorded By |)98/ |
| • | 0.5 | NA | NA NA | NA | Sw | Sw | 2/6 |
| (0 | | 24 | 2.0 | 1.0 | 1/20 | 170 | 2/7 |
| <u> </u> | | 48 | /.0 | 7.0 | dil | Pun | 2/8 |
| 1 | 0.5 | NA | NA | NA | R | R | 2/9 |
| 1 | | 24 | 2.0 | 1,0 | NDQ | سک | 2/10 |
| | | 48 | 1.02 | 1.0 | Ru | R | 2/11 |
| | 0.5 | · NA | NA | NA | NZA | ma | 2111 |
| 8. | | 24 | 1.00 | 1.0 | Sel | IJR | -2-12 |
| U | | 48 | 1.05 | | 770 | 1 50 | 2/3 |
| | 0.5 | NA. | NA. | NA | Sw | سحا | 3/13 |
| 1 9 | | 24 | 1,0D | 0 | HH | ·HH | 3/14 |
| · | | 48 | 1.0 5 | 0 | ŚĠ | <u> </u> | 2-15 |
| Challenge | 0.5 | na. | NA | NA | JP | R | 2/27 |
| Dase | | 24 | 0 | 0 | 77 | T | 2/28 |
| |] | 48 | 0 | 0 | Sold | de | 3/1 |

a - Dosage applied by technician indicated
 NA - Not Applicable

D=DOSQUAMATION Co 2/11/81

| Date A | nimal Received | 1/16/81 | - | 1 | Date Initiate | d 1/26/ |
|-------------|------------------|----------------|------------|----------------------|---------------------------|--|
| NA | Positive Control | | | | Animal No. | |
| \boxtimes | Test Group: | RT No. 816079 | Vehicle(), | 9% Soline Sterile | Test Varion Material LOTA | 50{1 22 <u>10. V20 10</u> 70 WIV |
| | DERTIAL_3 | ENSTITUM STUBI | IN GUINEA | PIGS | _ | |

Challenge Date 2/27

| | • | | | | | | |
|------------------------------|------------------------|----------------------------|----------|-------|-------------|-------------|--------|
| Sensi- tizing Dose No. | Dose ² (ml) | Obser- vation Period | Erythema | Edema | Technic lan | Recorded By | Date |
| | 0.5 | (Hrs) | | | | | 1981 |
| , - | 0.0 | NA NA | NA NA | NA. | 144 | THI | 126 |
| / | 1 | 24 48 | ļ | 8 | 30 | 1 500 | 1/27 |
| | <u> </u> | 40 | 0 | 1 0 | <u> </u> | 1 HM | 1/28 |
| 0 | 0.5 | NA | NA | NA_ | нн | нн | 1/28 |
| 2 | | 24 | 0 | D | 714 | 777 | Y 29 |
| | | 48 | 0 | 0 | -SW | Sw | 1/30 |
| | 0.5 | · NA | . AM | NA | m | no | 1/30 |
| 3 | | -24 | 0 | 0 | JP | 157 | 1/31 |
| \sim | | . 48 | 0 | 0 | TY | IR | 2/, |
| , 1 | 0.5 | NA | NA. | NA | R | R | 3/2 |
| 7 | • | 24 | . 0 | 0 | | ·HH | 1 -43_ |
| | | 48 | 0 | 0 | NOW | <u>: Co</u> | 2/4 |
| 5 | 0.5 | na_ | NA | NA. | 44 | HH | 2/4 |
| | | 24 | \circ | 0 | 202 | MA | 2/5 |
| | 1 | 48 | 0 | 0 | 50 | 156 | 2-50 |

a - Dosage applied by technician indicated
 NA - Not Applicable

Source Dean Daul Sex d

| ERIAL SENSITIZATION STORT | IN GOTHER PIGS |
|------------------------------|--|
| Test Group: RT No. 816079 | vehicle 0,9% Soline Material LOTNO, V201077 Sterile (1% W/V) |
| NA Positive Control Group NA | Vehicle NA Animal No. 0023 |
| Date Animal Received ///6/8/ | Date Initiated 1/26/8/ |
| Source Dean Daul Sex d | Challenge Date 2/27/8 |
| | |

| | • | | | | Tec | ₹. | |
|------------------------------|---------------------------|-------------------------------------|----------|-------|-------------|-------------|-----------|
| Sensi- tizing Dose No. | Dose ² (ml) | Obser- vation Period (Hrs) | Erythema | Edema | thn1c (en | Recorded By | Date 1981 |
| 6 | 0.5 | NA | NA. | NA | Sw | Sw | 2/6 |
| | | 24 48 | 0 | 0 | ADQ gryp | 100 | 2/7 |
| | 0.5 | NA. | NA. | NA | R | 100 | 2/9 |
| 7 | | 24 48 | 0 | 0 | NON | Sw | 2/4 |
| | 0.5 | · NA | NA | NA | PEU | 121 | 2111 |
| 8 | | 24 48 | 0 | 3 | She Chil | 1 JR | 2/13 |
| 9 | 0.5 | NA | NA. | NA | Sw | 150 | 2/13 |
| / | | 24 48 | 0 | 0 | 44 | 1 44 | 2-15 |
| Challenge | 0.5 | NA | NA | NA | R | R | 2/27 |
| Challenge Dose | | 24 48 | 0 | 0 | JP 740 | 77 | 3/1 |

a - Dosage applied by technician indicated
 NA - Not Applicable

| | DERMAL | SENSITIZATIO | N STUDY IN GUI | NEA PIGS | | \ / | | . , . |
|------------------------------|------------------------|-------------------------------------|----------------|----------|-----------------------|----------------------------|----------------------------------|----------------|
| Test | : Group: | RT No. 816 | 079 Vehicl | e0,9% Sa | <u>line</u> Mat 12 | t V(erial ² | 25,501 D <u>TNO.V</u> C170 | 1 6 20 W |
| NA Posi | itive Contr | ol Group | Z Vehic | le NA | An | 410 | 10. <u>00</u> 2 | 2 2 |
| | | 1/16/81 | | | Date | Initi | ated //_ | 24 |
| Source | Dean D | aul Sex | | • | Chall | enge D | ate 2/ | 2 |
| | | | | | | | | |
| | | | | | Teci | Rec | | |
| Sensi- tizing Dose No. | Dose ² (ml) | Obser- vation Period (Hrs) | Erythema | Edema | inic <u>lan</u> | Recorded By | Date 1981 | |
| | 0.5 | NA | NA | NA | HH | 11;11 | ااعره | |
| / | | 24 48 | 0 | 0 | HH | 1 HH 1 | 1/27 | |
| 2 | 0.5 | NA | NA | NA . | HH | H | 1128 | |
| 4 | | 24 | 0 | | HH | HH | Y29 | ı |

NA

NA

NA Ø

0

0

2

479 1/30

1/30

1/31

2/4

2/4

110 IX

M

HH

NA

00

NA

0

NA

0.5

0.5

0.5

24 48

NA

24

48

NA 24

48

NA

24 48

a - Dosage applied by technician indicated

NA - Not Applicable

| | 00.000 | DITOLLACATI | .011 01001 | IN GOINER | FIGS | | 11. | |
|-------------|------------------|-------------|------------|-----------|----------|-----------------|------------------------------------|--------------------------------|
| \boxtimes | Test Group: | RT No. 81 | P7001 | VehicleO | 9% Salin | Test Materia | Varisol 120 <u>140.V</u> 176 | 1 222- <u>20107</u> w/v) |
| NA | Positive Control | Group | NA | _ Vehicle | NA | _ Animal | 0- No. 00 | 22 ' |
| | nimal Received | | | | | Date Ini | tiated // | 26/8/ |
| Source | Deon Da | <u>u/</u> s | ex <u></u> | | | hallenge | Date 2 | /27/8 |
| | • | | | | a | | | ר |
| | | | | | ech | Reco | | |

| | | | | | Tech | Reco | |
|------------------------------|---------------------------|-------------------------------------|----------|-------|--------------------|-------------|-----------|
| Sensi- tizing Dose No. | Dose ² (ml) | Obser- vation Period (Hrs) | Erythema | Edema | <u>Cechnic Lan</u> | Recorded By | Date /98/ |
| 6 | 0.5 | NA | NA | NA | Sw | Sw | 2/6 |
| | | 24 | 1.0 | 0 | 400 | 1 740 | 2/2 |
| | | 48 - | ٥ | 0 | del | PCNI | 2/8 |
| | 0.5 | NA | NA. | NA | R | 12 | 2/9 |
| 7 | | 24 | 0 | O | NIA | Sw | 3/10 |
| 1 | | 48 | 0 | 0 | Go | Co | 2/11 |
| C | 0.5 | · NA | NA | , na | אכט | 200 | 2111 |
| X | | -24 | 0 | 0 | 440 | 198 | 2-12 |
| | | 48 | 0 | 0 | PP | سکرا | 2/13 |
| G | 0.5 | NA | NA. | NA. | Sw | Sw | بور/ح |
| 1 7 | | 24 | | 7 | 1111 | ·HH | 2/14 |
| , | | 48 | 0 | 0 | حاک | ي ڪي | 2-15 |
| Challenge Dose | 0.5 | NA | NA | NA | R | R | 2/27 |
| Dose | | 24 | 0 | 0 | 7 | 17 | 2/28 |
| 1 | 1 | 48 | 0 | 0 | del | mo | 3/1 |

a - Dosage applied by technician indicated
 NA - Not Applicable

| | DERMAL | SENSITIZATION STU | Y IN GUINEA PIGS | |
|--------|--------|-------------------|------------------------|---|
| Test 0 | Froup: | RT No. 816079 | Vehicle 0,9% Soline Ma | est Vorisofi 222. Sterial LO <u>TNO, V20</u> 102 |

| | | Sterile (| 170 W/V |
|-------------------------|--------------------|-------------------|----------|
| NA Positive Control Gro | up <u>NA</u> Vehic | tle NA Animal No. | 2021 |
| Date Animal Received | 16/81 | Date Initiate | d 1/26/8 |
| Source Dean Daul | Sex | Challenge Date | 2/27/ |

| | | | | | Tech | Reco | D |
|------------------------------|------------------------|-------------------------------------|----------|-------|--------------------|-------------|-----------|
| Sensi- tizing Dose No. | Dose ² (ml) | Obser- vation Period (Hrs) | Erythema | Edema | <u>Cechnic Lan</u> | Recorded By | Date 1981 |
| , . | 0.5 | NA | NA | NA | 44 | HH | 1/20 |
| / | | 24 48 · | 0 | 0 | MH | 1 5W | 1/27 |
| | 0.5 | NA | NA | NA NA | нн | 144 | 1/28 |
| 2 | | 24 48 | 0 | 00 | 71H Sw2 | HH | 1/30 |
| | 0.5 | ' NA | NA NA | NA · | m | 130 | 430 |
| 3 | | 24 48 | 1.0 | 0 | 45 | 157 | 1/31 |
| . 1 | 0.5 | NA | NA | NA. | R | P | 2/2 |
| 4 | • | 24 <i>-</i> 48 | 00 | 0 | HH | HH | 4/3 |
| 5 | 0.5 | NA | NA | NA | 44 | HH | 914 |
| | | 24 | 1.0 | 0 | 1170 | NX So | 2/5 |

a - Dosage applied by technician indicated
 NA - Not Applicable

| Test Group: | RT No. 816079 | vehicle0,9% So | Test Varisoff 222- <u>Jine Material LOTNO, V20102</u> 1e (170 w/v) |
|------------------------------------|---------------|----------------|--|
| NA Positive Cont | rol Group NA | Vehicle | Animal No. 002/ |
| Date Animal Received Source Dean Z | | · · | Date Initiated 1/26/8 |
| • | | | • |

| | | | | • | Tech | Rec | |
|------------------------------|---------------------------|-------------------------------------|----------|--------|-------------|-------------|-----------|
| Sensi- tizing Dose No. | Dose ² (ml) | Obser- vation Period (Hrs) | Erythema | Ed ema | Cechnic Lan | Recorded By | Date 1981 |
| , • | 0.5 | NA | NA | na | Sw | Sw | 2/6 |
| 6 | | 24 | 1.0 | 1.0 | 100 | (July | 2/7 |
| | | 48. | 4.0 | J | Japa . | WA | 12/8 |
| 7 | 0.5 | NA | NA | NA | R | R | 2/9 |
| / | | 24 | 1.0 | 0 | NOA | Su | 2/10 |
| | | 48 | 1.0 | 0 | co | Co | 2/1/ |
| 0 | 0.5 | · NA | NA : | NA | N28 | M2 | 2/11 |
| X | | 24 | 1.0 | 0 | 140 | 1 11 | 2-12 |
| | | 48 | 0 | 0 | de | 150 | 2/13 |
| 0 | 0.5 | NA | NA | NA. | لىتك | سک | 2/13 |
| 7 | | 24 | 0 | | HH | HH | 2114 |
| | | 48 | 0 | 0 | 56 | <u> </u> | 2-15 |
| Challenge Dose | 0.5 | NA | NA | NA. | R | T | 2/37 |
| DOSE | | 24 | 0 | 0 | 7 | 1 37 | 7/64 |
| | 1 | 48 | 0 | 0 | 1/20 | mo | 3/1 |

a - Dosage applied by technician indicated
 NA - Not Applicable

| Test Group: RT No. 816079 Ve | |
|--|----------------------------|
| NA Positive Control Group NA V | Vehicle NA Animal No. 0020 |
| Date Animal Received //16/81 Source Dean Daul Sex | Date Initiated //26/3 |

| | • | | | | | | |
|------------------------------|------------------------|-------------------------------------|----------|-------|-------------|-------------|--------------|
| | | | 1 | | Technic Lan | Recordud | Date |
| Sensi- tizing Dose No. | Dose ² (m/) | Obser- vation Period (Hrs) | Erythems | Edema | clan | hid By | 1981 |
| , . | 0.5 | NA | NA . | NA | HH | НН | ااعبه |
| / | | 24 48 | 0 | 0 | 149 HH | SW | 1/27 |
| 2 | 0.5 | NA | NA | NA NA | нн | HH | 1/28 |
| 2 | | 24 48 | 0 | 0 | HH Sw | HH H | 1/29 1/30 |
| .3 | 0.5 | NA - | NA . | NA | np | مرم | 130 |
| <u> </u> | | 24 48 | 00 | 0 0 | 100 | 1 | 1/31 |
| 4 | 0.5 | na | NA | NA | R | SP | 3/2 |
| <i>.</i> | · | 24 48 | 0 | 0 | ACA ACA | HH! | 2/3 2/4 |
| (5 | 0.5 | na | NA | NA. | HH | 1 | 2)4 |
| | | 24 48 | <u></u> | 0 | 100 56 | | 2/5 |

a - Dosage applied by technician indicated
 NA - Not Applicable

| Test Group: | RT No. 816079 | Vehicle 0,9% Soline Mater Sterile | Varisoft 222 Cial LOTNO, V2010 |
|----------------------|---------------|-----------------------------------|-----------------------------------|
| NA Positive Control | Group NA | Vehicle NA Anim | No. 0020 |
| Date Animal Received | | Date I | nitiated 1/26/8 |
| Source Dean Day | 4/ Sex | Challen | ge Date 2/27/ |

| | | | | | Tech | Rec | L |
|------------------------------|---------------------------|-------------------------------------|-----------|-------|-------------|-------------|-----------|
| Sensi- tizing Dose No. | Dose ² (mi) | Obser- vation Period (Hrs) | Erythema | Edema | Cechnic Lan | Recorded By | Date 1981 |
| , . | 0.5 | NA | NA | NA | SW | Sw | 2/6 |
| \mathcal{O} | | 24 | 0 | 0 | 1/70 | du | |
| | | 48 · | 0 | 0 | m | IALIN | 2/8 |
| 1 | 0.5 | NA | NA | NA | R | 1 R | 2/9 |
| 1 | | 24 | 0 | 0 | NEW | 5m | 2/10 |
| · | | 48 | <u>O'</u> | 0 | Co | Co | 2/11 |
| Q | 0.5 | . NA | NA . | NA | NOO | · | 2/11 |
| 8 | - | 24 | 0 | 0 | 44 | JR | 2-12 |
| | | 48 | . 0 | 0 | 140 | Su | 3/13 |
| 9 | 0.5 | NA | NA. | NA | | שט | 2/13: |
| / | | 24 | 0 | ٥ | HH | 44 | 2114 |
| , | | 48 | 0 | 0 | ડહ | | 2-15 |
| Challenge Dose | 0.5 | NA | NA | NA | SP | R | 2/27 |
| vose 1 | L | 24 | 0 | 0 | TP | 37 | 2/28 |
| | <u> </u> | 48 | 0 | 0 | 140 | 130 | 3/1 |

a - Dosage applied by technician indicated NA - Not Applicable

| Test Group: | RT No. 816079 | vehicle0,9% Saline Sterile | Test VariSof1 222- Material LO <u>TNO, V20107</u> (170 W/V) |
|----------------------|---------------|-------------------------------|---|
| NA Positive Control | Group NA | Vehicle NA | Animal No. 00/9 |
| Date Animal Received | | _ | Date Initiated 1/26/8/ |
| Source Dean Day | 4/ Sex | | hallenge Date 2/27/8 |

| | | • | | | (ech | Rec | |
|------------------------------|---------------------------|-------------------------------------|----------|-------|------------------|-----------------|------------|
| Sensi- tizing Dose No. | Dose ² (ml) | Obser- vation Period (Hrs) | Erythema | Edema | Cechnic Lan | Recorded By | 1981 |
| , • | 0.5 | NA | NA. | NA | HH | HH | 11210 |
| / | } | 24 48 · | 8 | 18 | M | 1 SW | 1/27 |
| 2 | 0.5 | NA | NA | NA NA | HH | HH | 1/28 |
| 2 | | 24 48 | 0 | 0 | ナナ | 44 | 1179 |
| 2 | 0.5 | 'NA | NA | NA. | Sw Ap | Sw | 1/30 |
| J | · | 24 48 | . 0 | 0 | 25 | 33 | 1/31 |
| , | 0.5 | NA | NA. | NA. | P | JP. | 2/2 2/2 |
| 7 | | 24 | S | 0 | 77 | 77 | 2/3 |
| 5 | 0.5 | NA NA | NA | NA. | • | Ea | 2/4 |
| 5 | | 24 48 | Ö | 2 | 111 122 56 | 95 VX8 TT | 2/5 |

a - Dosage applied by technician indicated
 NA - Not Applicable

| Source | Dean Da | ul Sex | 7 | | | allenge Dero 2/27/ |
|--------|------------------|-------------|------|----------|----------------------|-----------------------------------|
| Date A | nimal Received | | | | r | Date Initiated 1/26/8 |
| NA | Positive Control | Group NA | v | ebicle . | NA | Artifal No. 0019 |
| \sim | Test Group: | RT No. 2100 | Y ve | hicleO, | 1% Soline Sterile | Material LOTNO, V2010 (176 W/V |

| | , | | | | Tech | Rec | L |
|------------------------------|---------------------------|-------------------------------------|----------|-------|-------------|-------------|--------------|
| Sensi- tizing Dose No. | Dose ⁴ (ml) | Obser- vation Period (Hrs) | Erythema | Edema | Technic Lan | Recorded By | 1981 |
| , . | 0.5 | NA | NA | NA | Sw | Sw | 2/6 |
| 6 | | 24 48 · | 0 | 8 | NTR | 140 | 2/2 |
| 1 | 0.5 | . NA | NA NA | NA NA | R | INDR IR | 2/8 |
| / | - | 24 48 | 1.0 | 1.0 | ADA | Sw | 3/10 |
| 0 | 0.5 | NA | NA . | NA NA | NJA | 129 | 2/11 |
| 0 | | 24 48 | 00 | 0 | 130 | اعلا | 2-12 |
| | 0.5 | na | NA | NA. | Sw | سعا | 2/13 |
| : 7 | | 24 48 | - O | 90 | 70 30 | 1 56 | 2/14 2-15 |
| Challerge | 0.5 | NA | NA NA | NA | B | JR | 2/27 |
| Dose | | 24 | 0 | 0 | 131 | 70 | 3/1 |

a - Dosage applied by technician indicatedNA - Not Applicable

| Test Group: | RT No. 816079 | VehicleO, | 9% Saline | Test VariSoft 222 Material LOTNO, V2010 (176 W/V |
|----------------------|-----------------|-----------|-----------|--|
| NA Positive Control | | Vehicle | NA | Afficial No. 00/8 |
| Date Animal Received | | | D | ate Initiated //26/8 |
| Source Dean Date | 4/ Sex <u>d</u> | | Ch. | allenge Date 2/27/ |

| | | | | | Tech | Rec | L |
|------------------------------|---------------------------|-------------------------------------|----------|-------|-------------|-------------|--------------|
| Sensi- tizing Dose No. | Dose ² (ml) | Obser- vation Period (Hrs) | Erythema | Edema | Cechnic Lan | Recorded By | 1981 1981 |
| , • | 0.5 | na | NA. | . NA | 44 | 111 | |
| | | 24 48 | 0 | 10 | M | 1500 | 1/27 |
| | 0.5 | . 40 | -0 | 10 | ו אא | 1 MM | 1728 |
| 2 | 0.5 | NA | NA. | NA | НН | НН | 1/28 |
| _ | 1 1 | 24 | 0 | 0 | HH | HH | 1/29 |
| | 1 | 48 | | 0_ | Sw | Sw | 1/30 |
| . 3 | 0.5 | . NA | NA | NA | de | 130 | 1/30 |
| | | 24 | | Lo | JE | 100 | 1/31 |
| | | 48 | 0 | 0 | 37 | 1 12 | 2/1 |
| 4 | 0.5 | NA | NA | NA. | R | TP | 2/2 |
| | · | 24 | . 0 | D | | HH | 2/3 |
| • | <u> </u> | 48 | | 0 | | Co | 2/4 |
| 5 | 0.5 | NA | NA | NA | 7 | HH | 2/4 |
| | 1 L | 24 | | ٥ | NUR | AUR | 2/5 |
| | <u> </u> | 48 | | 0 | 36 | داک | 2-60 |

a - Dosage applied by technician indicated
 NA - Not Applicable

| \boxtimes | Test Group: | RT No. 81607 | QvehicleO | 9% Saline Sterile | Test Variation | 50f1 222- NO. V20102 170 W/V |
|-------------|------------------|---------------|-----------|----------------------|----------------|------------------------------------|
| NA | Positive Control | | Vehicle | NA | Animal No. | 0018. |
| | nimal Received | | | | Date Initiate | ed 1/26/8 |
| Source | Dean Da | <u>и/</u> Sex | <u>~</u> | · | hallenge Date | 2/27/8 |

| | | • | | | Tech | Rec | |
|------------------------------|---------------------------|-------------------------------------|-----------|-------|----------------|-------------|-----------|
| Sensi- tizing Dose No. | Dose ¹ (ml) | Obser- vation Period (Hrs) | Erythema | Edewa | Cechnic Lan | Recorded By | Date 1981 |
| , • | 0.5 | NA | NA. | NA. | Sw | Sw | 2/6 |
| 0 | | 24 48 | 1.0 | 0 | 100 | 1440 | 2/7 |
| | 0.5 | 48. | 1.0 | /.0 | det | LALAN ! | 2/8 |
| 7 | 0.5 | NA | NA | AM | SR | IR | 2/9 |
| ./ | | 24 | 0 | O | NOX | Su | 2/10 |
| | <u> </u> | 48 | 0 | 0 | Co | Co | 2/4 |
| C | 0.5 | · NA | NA | NA NA | PCN | KU | 2/11 |
| X | | 24 | , O | 0 | 14 | IJR | 2-12 |
| | . : | 48 | ن ا | O | 147 | البيكا | 2/13 |
| Q | 0.5 | NA · | NA | NA. | Sw | . Sw | 2/13 |
| 7 | | 24 . | 0 | 0 | 111 | ナナ | भाप |
| <u> </u> | ! | . 48 | . 0 | Ò | فك | : 56 | 2.15 |
| Challenge Dose | 0.5 | . NA | NA | NA | B | 57 | 2/27 |
| 12050 | | 24 | Ò | 0 | 3 | 7 | 3/28 |
| | <u> </u> | 48 | 0 | 0 | del | 190 | 3/1 |

a - Dosage applied by technician indicatedNA - Not Applicable

| \bowtie | Test Group: | RT No. | 81100 | 74_ | VehicleO, | 4% Salii Steriil | Material LOT | 170 W/V |
|-----------|------------------|--------|---------|-----|-----------|---------------------|----------------|----------|
| NA | Positive Control | Group | NA | | Vehicle | NA | Animal No. | 0017 |
| | nimal Received | | | | _ | | Date Initiate | d 1/26/8 |
| Source | Deon Da | ul | _ Sex _ | 3 | | • | Challenge Date | 2/271 |

| | | | | | Tech | Rec | |
|------------------------------|------------------------|-------------------------------------|----------|------------|--------------------|-------------|------------|
| Sensi- tizing Dose No. | Dose ² (ml) | Obser- vation Period (Hrs) | Erythema | Edema | <u>Technic Lan</u> | Recorded By |)48I |
| , . | 0.5 | NA | NA | N A | ## | нн | اجله |
| / | | 24 48 · | 8 | 0 C | NH | 1 SW | 1/27 |
| 2 | 0.5 | NA | NA | NA. | нн | НН | 1/28 |
| 1 | | 24 48 | 0 | 0 | רויב אא | HH Sw | 1/29 |
| 3 | 0.5 | · NA | NA . | NA. | AD. | 130 | y30 |
| | i | 24 48 | 1.0 | 0 | المار | JP JP | 1/3/ |
| 4/ | 0.5 | NA 1 | NA. | NA NA | P | F | 3/2 |
| 7 | | 24 48 | 8 | . 8 | VDX) HH | 44 | 2/3 2/4 |
| .5 | 0.5 | NA | NA | NA | 44 | 手 | 2/4 |
| | | 24 48 | 0 | 0 | NJA | N/N SG | 2/5 |

a - Dosage applied by technician indicated
 NA - Not Applicable

| Test Group: | RT No. 816079 | Vehicle 0,9% Soli | Test VOI SOF 1222 <u>Me Material LOI NO. V2010</u> E (170 W/V |
|----------------------|---------------|-------------------|--|
| NA Positive Control | Group NA | _ Vehicle _ NA | Animal No. 00/7 |
| Date Animal Received | | | Date Initiated 1/26/8 |
| Source Dean Da | u/ Sex | | Challenge Date 2/27/ |

| | | | | | Tech | Rec | L |
|------------------------------|---------------------------|-------------------------------------|---------------|-------|-------------|-------------|-----------|
| Sensi- tizing Dose No. | Dose ² (mi)··· | Obser- vation Period (Hrs) | Erythema | Edema | Cechnic Lan | Recorded By | Date /98/ |
| , . | 0.5 | NA | NA. | NA | يسك | Sw | 2/6 |
| | | 24 | 1.0 | 1.0 | 1200 | 179 | 2/2 |
| | | 48 | .0 | 10 | del | MON | 12/8 |
| . 7 | 0.5 | NA | NA | NA | R | IR | 2/9 |
| 1 | | 24 | 0 | 0 | PCU | Ju | 2/10 |
| | | 48 | 0 | 0 | CO | Co | 2/11 |
| Ω | 0.5 | NA NA | na | NA | NJA | NZU | 211 |
| 8 | | 24 | 0 | 0 | 447 | 178 | 2-12 |
| | | 48 | 1.0 | 0 | de | | 2/13 |
| 9 | 0.5 | NA | NA : - | NA | لىنك | Sw | 2/13 |
| . / | 1 | 24 | | 0 | HH | HH | 2114 |
| | <u> </u> | 48 - | . 0 | 0 | 56 | : 56 | 2-15 |
| Challenge Dose | 0.5 | NA | NA | NA | R | 177 | 2/27 |
| LOSE ' | 1 | 24 | 0 | 0 | 18 | 37 | 428 |
| | <u> </u> | 48 | 0 | 0 | M | 130 | 3/1 |

a - Dosage applied by technician indicated
 NA - Not Applicable

| Test Group: | PT No. 816079 | VehicleO,C | 1% Soline Mate: | VO.FISO 11220 100.V2010 1130 mly |
|----------------------|-----------------------|-------------|-----------------|--|
| NA Positive Control | Group NA | _ Vehicle _ | NA Ani | 410- Mai No. 0016 |
| Date Animal Received | | | Date 1 | Initiated 1/2/6/3 |
| Source Dean Da | <u>и/</u> Sex <u></u> | - | Challer | nge Date <u>2/27</u> |
| | | | | |

| | | | | | Tech | Rec | 6 |
|------------------------------|---------------------------|-------------------------------------|----------|-------|-------------|-------------|-------------|
| Sensi- tizing Dose No. | Dose ² (mi) | Obser- vation Period (Hrs) | Erythema | Edema | [echnic Lan | Recorded By | Date . 1981 |
| , • | 0.5 | NA | NA | NA | нн | нн | 1120 |
| / | | 24 48 | 0 | Q | 5W | 15W | 1/27 |
| | 1 4 | 46. | | ۵ | 1 HH | ואא | Y28 |
| 0 | 0.5 | NA | NA | NA | нн | нн | 1/28 |
| 2 | | 24 | 0 | C | NN | HH | 1/39 |
| | | 48 | 0 | 0 | Sw | ليكا | 1/30 |
| _ | 0.5 | . NA | na . | NA NA | m | no | 1/30 |
| 3 | | 24 | Ð | 0 | J. | 1 JP | 1/81 |
| | | 48 | | 0 | 150 | 1 7 | 2/1 |
| 41 | 0.5 | NA | NA - | NA. | JP | P | 2/2 |
| . 7 | | 24 | 1.0 | D | HH | . H. | 43 |
| | | 48 | 1.0 | 0 | NTD | :Co | 2/4 |
| 5 | 0.5 | NA. | NA | NA | НН | 11 | 2/4 |
| | | 24 | 1.0 | a | NJO | M | 2/5 |
| | 1 | 48 | 1,0 | 0 | 56 | 156 | 2-6 |

a - Dosage applied by technician indicated
 NA - Not Applicable

| Test Group: | RT No. 816079 | VehicleO, | 1% Saline | Test Varisof1 222 Material LOTNO, V2010 (17 W/V |
|----------------------|-----------------|-------------|-----------|---|
| NA Positive Control | Group <u>NA</u> | _ Vehicle . | NA | Animal No. OON |
| Date Animal Received | | | D | ate Initiated 1/26/8 |
| Source Dean Da | u/ Sex <u>3</u> | | Ch | allenge Date 2/27 |

| | | | | | Tech | Rec | |
|------------------------------|------------------------|-------------------------------------|----------|-------|-------------|-------------|--------------|
| Sensi- tizing Dose No. | Dose ² (ml) | Obser- vation Period (Hrs) | Erythema | Edema | Cechnic Lan | Recorded By | Date /98/ |
| , • | 0.5 | NA | NA. | NA | Sw | Sw | 2/6 |
| 6 | | 24 | 1.0 | 0 | 120 | 100 | 2/2 |
| | | 48 | | ٥ | 100 | 1400 | 2/8 |
| 4 | 0.5 | NA | NA | NA. | R | IR | 2/9 |
| / | | 24 | 0 | 0 | PCV | Sw | 2/10 |
| • | | 48 | 0 | 0 | Co | Co | 2/11 |
| C | 0.5 | . NA | NA | NA | PCU | un | 2/11 |
| X | | -24 | G | . 0 | del | الملا | 2-12 |
| 0 | <u> </u> | - 48 | 0 | ð | 140 | 1 500 | 2/13 |
| a | 0.5 | NA | NA. | NA | ربيک | Sw | ور/د |
| 7 | ·. | 24 . | 0 | 00 | 144 | エエ・ | BIIL |
| | | 48 | 0 | D | 56 | 1:56 | 2-15 |
| Challenge Dose | 0.5 | NA | na | NA | R | P | 2/27 |
| 12050 | | 24 | 0 | 0 | JP | IF | 428 |
| | <u> </u> | 48 | 0 | 0 | del | ded | 3/1 |

a - Dosage applied by technician indicated NA - Not Applicable



P.O. Bex 7545 • Madison, Wisconsin 53707 • 608/241-4471

A Division of Relaton Purine Company

GUINEA PIG MAXIMIZATION STUDY OF VARISOFT 222-90% (LOT NO. V2010225)

SPONSOR: SHEREX CHEMICAL COMPANY

DUBLIN, OH 43017

STUDY NO.

816079

INITIATION: 1/5/81

COMPLETION: 1/29/81

REPORTED:

2/24/81

SAMPLE: Varisoft 222-90% (Lot No. V2010225)

ENCLOSED: METHOD, PAGE 2 AND 3

SUMMARY, PAGE 4 RAW DATA APPENDIX

SIGNED:

TECHNICAL SUPERVISOR

HEAD, ACUTE TOXICOLOGY

STUDY DIRECTOR

BY AND FOR RALTECH SCIENTIFIC SERVICES

RAW DATA FOR THIS STUDY IS KEPT ON FILE AT RALTECH SCIENTIFIC SERVICES, MADISON, WISCONSIN.

3301 KINSMAN BLVD. • P.O. BOX 7545 • MADISON, WISCONSIN 53707 • PHONE (608) 241-4471 • TLX 260098 HAZRAL MDS

Guinea Pig Maximization Study Test Material Varisoft 222-90% (Lot No. V2010225) Study No. 816079

Sponsor

Sherex Chemical Company P. O. Box 646 Dublin OH 43017

Principal Investigator

Robert L. Harrison

Contractor

Hazleton Raltech, Inc. 3301 Kinsman Boulevard Madison WI 53704

Study Director

Gary W. Thompson, BS

Amendment No. 1 to the Report

Reason

The stated volume of the dose was incorrect and the method of application of the test substance during intradermal injections was not clarified in the "Method" section of the final report.

Change

The Method section on page 2 of the final report, sentence 2, should be corrected to read:

"...one row on each side of the midline as follows: 0.05 ml of the prepared Freund's Adjuvant Solution 0.05 ml of the 5% aqueous test solution, and 0.05 ml of the 5% solution of test material and Freund's Adjuvant Solution."

Gary W. Thompson, BS

Study Director, Acute Toxicology

6-4-82

Date

by and for Hazleton Raltech, Inc.

/dka



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A Division of Relation Purine Company

RT LAB NUMBER 816079 GUINEA PIG MAXIMIZATION

PAGE 2

Test Material: Varisoft 222-90% (Lot No. V2010225)

Test Animal: Young adult male guinea pigs were procured, maintained individually in stainless steel cages in temperature and humidity controlled rooms, provided continuous access to Purina Guinea Pig Chow and water and held for a conditioning period of at least 7 days.

Test System: Ten male guinea pigs weighing between 458 and 496 grams were chosen at random and used for this study. The animals were individually housed and identified by animal number and ear tag.

Preparation of Test Material: For the intradermal injections the Freund's Complete Adjuvant Solution was prepared by adding 5.0 mL of sterile water for injection in 1.0 mL increments to 5.0 mL of Freund's Adjuvant.

The 5% solution of test material in sterile water was prepared by taking 0.5 gram of Varisoft 222-90% (Lot No. V2010225) and adding sterile water for injection to a total volume of 10.0 mL.

The 5% solution of test material in Freund's Adjuvant was prepared by placing 0.5 g of Varisoft 222-90% (Lot No. V2010225) into a 30-mL beaker and adding sterile water to a Q.S. volume of 5.0 mL. To this, 5.0 mL of Freund's Adjuvant was added in 1.0 mL increments while stiring.

For the topical induction the Varisoft 222-90% (Lot No. V2010225) was administered at a concentration of 50% w/v in sterile saline. For the challenge procedure, the test material was administered at a 1.0% w/v concentration in sterile saline.

Method: A 4.0 x 6.0 cm area was clipped along the midline over the shoulder region. Two rows of three-deep intradermal injections (total of 6 injections) were made within the boundaries of a 2.0 x 4.0 cm area, one row on each side of the midline as follows: 0.1 mL of the prepared Freund's Adjuvant Solution, 0.1 mL of a 5% aqueous test solution, and 0.1 mL of a 5% solution of test material and Freund's Adjuvant Solution.

One week after the injections, the same area was clipped and closely shaved with an electric razor. A 2.0 x 4.0 cm patch of Whatman No. 3 filter paper was saturated with a 50% w/v solution of Varisoft 222-90% (Lot No. V2010225) and sterile 0.9% saline, placed over the injection sites, then covered with an overlapping of Blenderm tape and secured by an overwrap of Elastoplast tape. The dressing remained in place for 48 hours.





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A Division of Relation Purine Company

RT LAB NUMBER 816079
GUINEA PIG MAXIMIZATION

PAGE 3

Two weeks after topical induction the animals received a challenge dose. The hair was removed from a $5.0 \times 5.0 \text{ cm}$ area on the flank by clipping and shaving as before. A 1.02 w/v solution of the test material in sterile 0.92 saline was applied on a $2.0 \times 2.0 \text{ cm}$ piece of filter paper in the same fashion as for topical induction. The patch was sealed to the flank for 24 hours under a 4.0 cm strip of Blenderm tape. Complete occlusion was made by an overwrap with Elastoplast tape wound around the trunk.

Observations: Twenty-four hours following patch removal the test sites were examined for erythema and edema. The sites were examined again at 48 hours after patch removal to detect weak, slowly developing reactions. The test sites were shaved 3 hours prior to the 24-hour reading. The reactions were scored according to the following 4-point scale:

- 0 = no reaction
- l = scattered mild redness
- 2 = moderate and diffuse redness
- 3 = intense redness and swelling

The important statistic in maximization testing is the frequency of sensitization, not the intensity.



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A Division of Reiston Punna Company

RT LAB NUMBER 816079 GUINEA PIG MAXIMIZATION

PAGE 4

Test Animal: Albino guinea pigs

Source: Dean Dahl, Luxemburg, Wisconsin

Date Animals Received: 12/23/80

Test Material: Varisoft 222-90% (Lot No. V2010225)

Date Test Started: 1/5/81

Date Test Completed: 1/29/81

| Animal Number | ·a | Challenge Dos | e Reactions |
|------------------|-------------|---------------|-------------|
| Mambel | Sex | 24 Hours | 48 Hours |
| 64000730 | м | 0 | |
| 64000731 | M | 0 | 0 |
| 64000741 | M | 0 | 0 |
| 64000746 | M | Ū | 0 |
| 64000750 | | 0 | 0 |
| | M | 0 | 0 |
| 64000751 | M | 0 | Ô |
| 64000752 | M | o | _ |
| 64000754 | M | · · | 0 |
| 64000757 | | 0 | 0 |
| | M | 0 | 0 |
| 64000759 | M | 0 | Ö |

General Behavior and Appearance:

All of the guinea pigs used in this study appeared normal throughout the study period. Normal body weight gains were recorded for all animals during the course of the study.

Skin Reactions to Varisoft 222-90% (Lot No. V2010225):

None of the ten guinea pigs exhibited a reaction to the challenge dose at either the 24 or 48 hour observations.

Conslusion:

Based upon the results obtained, the test material, Varisoft 222-90% (Lot No. V2010225), is not considered a skin sensitizer.

Reference:

Magnusson, B., MD, and A. Kligman, PhD, MD, Allergic Contact Dermatitis in the Guinea Pig, Charles C. Thomas, pub., 1970, pp. 113-117.

Dermal Sensitization In Guinea Pigs - Body Weights

| ~ | IXI | | | • |
|----------|-----|---------------------------|--------------|--------------|
|) | Щ | Test Group RT No. 8110079 | Vehicle LIC | |
| | 7 | | _N | |
| | | Positive Control Group | | |
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| | | | Animal | Number | | | | 7 | |
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| | | Animal Number | | |
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| 480 | 508 | Scale Used: K-Tron 4804 | | |
| 465 | | Scale Used: K-Tron 4809 | | hobs |
| 533 | 599 | Scale Used: K-Tron 4809 | | 1/17/21 |
| | | Scale Used: | انتک | 1/26/81 |
| _ | | Scale Used: | | |

NA - Not Applicable

GUINEA PIG MAXIMIZATION TEST

| | Test Compound Vari | 50f+ 227-91 | 7 105 10 | 996 4800b n.m. | |
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Scoring Code: 0 = Normal, No Reaction

L = Scattered Mild Redness

2 * Moderate and Diffuse Redness

3 = Intense Redness and Swelling

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Dermal Sensitization in Guinea Pigs - Daily Observations

Test Group RT No. 8110079 Vehicle NO Test Compound Vari Soft 222 Positive Control Group NO Vehicle NO Room No. 101 8 *

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S = Except salwation 1117181414 N - No Visible Abnormalities

NA - Not Applicable

*Test animals moved to 400m 3 on 1/15/81 NOA

Dermal Sensitization in Guinea Pigs - Daily Observations

Test Group RT No. 816079 Vehicle NA Test Compound Vorisoft 222-90

Lot No. V2010225

NA Positive Control Group NA Vehicle NA Room No. 11616

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N - No Visible Abnormalities

M& - Not Applicable

* Test animals moved to room 3 on 1/15/8/ NOO

Dermal Sensitization in Guineæ Pigs - Daily Observations

Test Group RT No. 8110079 Vehicle LA Test Compound Vari Soft 2774
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ROOM No. 11016 4

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N - No Visible Abnormalities

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Dermal Sensitization in Guinea Pigs - Daily Observations

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N - No Visible Abnormalities

NA - Not Applicable

* Test animals moved to room 3 on Ilisiai NO



P.O. Box 7545 • Madison, Wisconsin \$3707 • 608/241-4471 A Division of Raiston Purina Company

GUINEA PIG MAXIMIZATION STUDY OF VARISOFT 222-90 LOT #SC49-66A 644750

SPONSOR:

SHEREX CHEMICAL COMPANY

DUBLIN, OHIO

STUDY NO. 856938

INITIATION: 4/27/81

COMPLETION: 5/21/81

REPORTED:

6/3/81

SAMPLE:

VARISOFT 222-90 LOT #SC49-66A 644750

ENCLOSED: METHOD, PAGES 2 AND 3

SUMMARY, PAGE 4 RAW DATA APPENDIX

SIGNED:

TECHNICAL SUPERVISOR

GARY W. THOMPSON, BS

MANAGER, ACUTE TOXICOLOGY

STUDY DIRECTOR

BY AND FOR RALTECH SCIENTIFIC SERVICES

RAW DATA FOR THIS STUDY IS KEPT ON FILE AT RALTECH SCIENTIFIC SERVICES, MADISON, WISCONSIN.

KT LAB NUMBER 856938 GUINEA PIG MAXIMIZATION

Test Material: Varisoft 222-90 Lot #SC49-66A 644750

Test Animal: Young adult male guinea pigs were procured, maintained individually in stainless steel cages in temperature and humidity controlled rooms, provided continuous access to Purina Guinea Pig Chow and water and held for an acclimation period of at least 7 days.

Test System: Ten male guinea pigs weighing between 448 and 500 grams were chosen at random and used for this study. The animals were individually housed and identified by animal number and ear tag.

Preparation of Test Material: For the intradermal injections the Freund's Complete Adjuvant Solution was prepared by adding 5 mL of sterile water for injection in 1 mL increments to 5 mL of Freund's Adjuvant.

The 5% solution of test material in sterile water was prepared by taking 0.25 gram of Varisoft 222-90 Lot #SC49-66A 644750 and adding sterile water for injection to a total volume of 5.0 mL.

The 5% solution of test material in Freund's Adjuvant was prepared by mixing 0.25 g of Varisoft 222-90 Lot #SC49-66A 644750 with 2.5 mL of sterile water and adding 2.5 mL of Freund's Adjuvant in 1.0 mL increments to a total volume of 5.0 mL.

For the topical induction and challenge procedures the test material was applied at 25% w/v and 1.0% w/v suspensions in 0.9% saline, respectively.

Method: A 4.0 x 6.0 cm area was clipped along the midline over the shoulder region. Two rows of three-deep intradermal injections (total of 6 injections) were made within the boundaries of a 2.0 x 4.0 cm area, one row on each side of the midline as follows: 0.05 mL of the prepared Freund's Adjuvant Solution, 0.05 mL of a 5% aqueous test solution, and 0.05 mL of a 5% solution of test material and Freund's Adjuvant Solution.

One week after the injections, the same area was clipped and closely shaved with an electric razor. A 2.0 x 4.0 cm patch of Whatman No. 3 filter paper was saturated with a 25% w/v suspension of test material in 0.9% saline, placed over the injection sites, then covered with an overlapping of Blenderm tape and secured by an overwrap of Elastoplast tape. The dressing remained in place for 48 hours.

Two weeks after topical induction the animals received a challenge dose. The hair was removed from a $5.0 \times 5.0 \text{ cm}$ area on the flank by clipping and

shaving as before. A 1.0% w/v suspension of test material in 0.9% saline was applied on a 2.0 x 2.0 cm piece of filter paper in the same fashion as for topical induction. The patch was sealed to the flank for 24 hours under a 4.0 cm strip of Blenderm tape. Complete occlusion was made by an overwrap with Elastoplast tape wound around the trunk.

Observations: Twenty-four hours following patch removal the test sites were examined for erythema and edema. The sites were examined again at 48 hours after patch removal to detect weak, slowly developing reactions. The test sites were shaved 3 hours prior to the 24 hour reading. The reactions were scored according to the following 4-point scale:

- 0 = no reaction
- 1 = scattered mild redness
- 2 = moderate and diffuse redness
- 3 = intense redness and swelling

The important statistic in maximization testing is the frequency of sensitization, not the intensity.

Test Animal: Albino guinea pigs Source: Dean Daul, Luxemburg, WI Date Animals Received: 4/10/81

Test Material: Varisoft 222-90 Lot #SC49-66A 644750

Date Test Started: 4/27/81

Date Test Completed: 5/21/81

| Animal Number | Sex | 24 Hours Right | 48 Hours Right |
|------------------|-------|-------------------|-------------------|
| . # | | | |
| 64100216 | M | 1 | 0 |
| 64100217 | M | ō | Ĭ |
| 64100218 | M | ŏ | 0 |
| 64100219 | M | 0 | 0 |
| 64100220 | M | 0 | 0 |
| 64100221 | M | 0 | 0 |
| 64100222 | M. | 0 | 0 |
| 64100223 | M M | 1 | 0 |
| 64100224 | M | 1 | 0 |
| 64100225 | | Ü | 0 |
| 07100223 | M | 0 | 0 |

General Behavior and Appearance:

All of the guinea pigs used in this study appeared normal throughout the study period. Normal body weight gains were recorded for five animals during the course of the study. Four guinea pigs exhibited a weight loss and one animal exhibited a slight weight gain at the end of the second week on test. Normal body weight gains were recorded for these animals at the one and three week weighings.

Skin Reactions to Varisoft 222-90 Lot #SC49-66A 644750:

Two animals (Nos. 64100216 and 64100223) exhibited a sensitization reaction to the test material at 24 hours following the challenge application. Both animals had a scattered mild redness of the test site at 24 hours. Eight guinea pigs did not exhibit any reaction to the challenge dose at either the 24 or 48 hour observations.

Conclusion:

Based upon the results obtained, the test material, Varisoft 222-90 Lot #SC49-66A 644750, is considered a skin sensitizer in guinea pigs.

Reference:

Magnusson, B. MD, and A. Kligman, PhD, MD, Allergic Contact Dermatitis in the Guinea Pig, Charles C. Thomas, pub., 1970, pp. 113-117.

GUINEA PIG MAXIMIZATION TEST

| Test Compound | Test Compound | | | | | | | |
|-----------------------|---------------|------------|-------------------|-----------------------|--|--|--|--|
| hu wearit | NA | 2044 120 | _ RT No. <u> </u> | | | | | |
| | | | Source Doan Doul | | | | | |
| Date of Intradermal I | njections 4/2 | 7/81 | | Technician Sw, MR NOR | | | | |
| | | Technician | | | | | | |
| Date of Challenge | 51.81 | | NDA 80. | | | | | |
| | | | | | | | | |
| | 24 Hour | 'S | 48 Hou | rs | | | | |
| Animal No., Sex | Right | Left | Right | Left | | | | |
| 64/0- 0216 8 | | | 0 | | | | | |
| 0217 0 | 0 | , . | 9 | | | | | |
| 0218 | 0 | | 0 | 1 | | | | |
| 0219 07 | 0 | | O | | | | | |
| 0220 A | 0 | | . 0 | | | | | |
| 0221 0 | 0 | | .0 | | | | | |
| 0222 0 | 0 | | 0 | | | | | |
| 0223 0 | | | 0 | | | | | |
| 0224 07 | 0 | | 0 | | | | | |
| 0225 67 | 0 | | 0 | 1 | | | | |
| Technician | Co | | A | | | | | |
| Recorded By | ER. | | R | | | | | |
| Date 1981 | 5/20 | | 56. | | | | | |

NA - NOT APPLICABLE

Scoring Code: 0 = Normal, No Reaction

1 = Scattered Mild Redness

2 = Moderate and Diffuse Redness

3 = Intense Redness and Swelling

| REVIEWED | BY: | NZO | | DATE: | 92918 |
|----------|-----|-----|--|-------|-------|
|----------|-----|-----|--|-------|-------|

Dermal Sensitization In Guinea Pigs - Body Weights

| \leftarrow | | | | | | | |
|--------------|-------------|----------------|-----------|--------------|------|------------------------|------|
| X | Test Group | RI No. 356935 | Vehicle _ | ALA_ | Test | Compound Var Co St | 222. |
| ごり | Positive Co | ntrol Group NA | Vehic | 1e <u>UN</u> | | LOT #SC 49-64 10447 | A |

| | | | Animal | Number | | | | 7 | •. |
|------|----------|-------|--------|--------|-------|--------|--------|--------|---------|
| 640- | 1921 3-1 | 6-10- | 640- | 6410- | 2410- | Delin- | E-110- | Tech- | |
| 0214 | 6217 | 0218 | 0219 | 0220 | 022/ | 02.22 | 0223 | nician | Date |
| 408 | 456 | 496 | 500 | 475 | 477 | 448 | 448 | NJO | 4/27/8 |
| 574 | 5/7 | 584 | 559 | 524 | 532 | Uq8 | 499 | no | 5/4/81 |
| 569 | 522 | 626 | 562 | 531 | 543 | 478 | 534 | xyyp | 5/11/81 |
| 770 | 618 | 691 | 028 | 637 | 628 | 573 | 619 | PMN | |
| | | | | | | | | | |
| | | | | | | | | | |

| , , | | Animal Number | | |
|------------------|------|--------------------------|-----------------|---------|
| 40- | 2000 | | | |
| C224 | 0225 | | Tech- nician | Date |
| 4 5 9 | -100 | Scale Used: K-TRON 4809 | Now | 4/27 81 |
| 528 | 512 | Scale Used: K. TRON 4809 | | 5/4/81 |
| 509 | 473 | Scale Used: K-Tron 4809 | destil | 5/11/81 |
| 595 | | Scale Used: K-TRON 4809 | 27 107 | |
| | | Scale Used: | | |
| | | Scale Used: | | |



Dose Range

| • | DERMAL SENSITIZATION STUDY | IN GUINEA PIGS |
|----------------|----------------------------|-------------------------------|
| Test Group: | RT No. 856938 Vehicle | Saline LOT = SC 49-669 644150 |
| | | Saline LOT = SC 49-669 644150 |
| Date Animal Re | ceived 4/3/81 | _ |
| Source | con Daul Sex 0 | Date Initiated 4/23/8/ |
| | | |

| | | | | | Tec | Re | |
|------------------------|-------------------|-------------------------------------|----------|-------|------------|-------------|--------|
| LOUTIO - ADIMAL NO. | Dose ⁴ | Obser- vation Period (Hrs) | Erythema | Edema | [ecluician | Recorded by | 1981 |
| 0129 | 0.5 | MA | na . | NA | Ray | ي ا | 4/23 |
| <u>(A)</u> | 1.0% | 24 48 | 0 | 0 | TP ST | 100 | : 4/24 |
| 0/29 | 0.5 | NA | NA | NA | NOO | ļ | 4/23 |
| B | 5.0% } | 24 | 1.0 | 1.0 | m | 50 | 424 |
| 0/29 | 0.5 | NA | NA | · NA | NOO | ER | 4/23 |
| (C) | 10.0%; | 24 48 | 2.0 | 1.0 | NO B | 100 | 4/24 |
| | | na | NA . | NA. | | 0 | 0 |
| | | 24 | | | | 7 | , |
| | | NA 24 | NA | KA | | | |
| | | 48 | | | | · · · | |

a - Dosage applied by technician indicated

NA - Not Applicable

O recording error 4/23/81 EL

Head

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

| Test Group: | RT No. 85 | 6938 | Venicle | Ster 10.0.9% | Material | Varisoft |
|-----------------|-----------|-------|---------|--------------|----------|----------|
| | | | | Salve | LOT # | SC-4966 |
| Date Animal Rec | eived | 3/81 | | • | | |
| Source Dean | Days | Sex _ | 7 | Date I | Ditiated | 4/23/81 |

| | | | | | <u>Tecl</u> | Rec | |
|------------------------------|-------------------|-------------------------------------|----------|-------|---------------------|-------------|------|
| 6410 - Animal No. Site | Dose ² | Obser- vation Period (Hrs) | Erythems | Edema | Technician | Recorded by | Ata |
| 0183 D | 0.5 | NA | NA | NA | NOR | NOV | 4/23 |
| @ | 10.0% | 24 48 | 1.0 | 1.0 | N70 | ALTO J? | 4/24 |
| 0/83 | 0.5 | MA | NA | NA | ATTO | | 4/23 |
| B | 1.0% | 24 48 | 0 | 0 | NZO | 157 | 4/24 |
| 0183 © | 0.5 | NA | MA | · KA | NOO | 1 | 4/23 |
| 0 | 5.0% | 24 | 2.0 | 2.0 | NUTO | 1/78 | 1/25 |
| | | NA | NA | NA | - X ¹ ., | - | 7/07 |
| | | 24 | | | | | |
| | | MA | ŅA. | KA | | | |
| | | 24 48 | | | | | |

a - Dosage applied by technicism indicated
 NA - Not Applicable

Head Tail

Dose Ranze

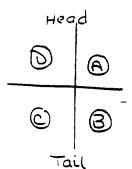
Source Dean Daul Sex 7

| | SENSITIZATION | STUDY IN GUINEA PIG | <u>s</u> |
|------------------|---------------------|----------------------|--------------------------------|
| Test Group: | RT No. 856938 | Vehicle Storile 0.9% | Test Material Varkof+ 222-9 |
| | | Saline | LOT#5C49-669644 |
| Date Animal Rece | eived <u>4/3/81</u> | | |

Date Initiated 4/33/81

| 1 /10- | | | ſ | | Teclmiciau | Reco | Da |
|------------------------------|-------------------|-------------------------------------|----------|-------|------------|-------------|------|
| 6410 - animal No. Site | Dose ⁴ | Obser- vation Period (Hrs) | Erythema | Edema | ician | Recorded By | 1987 |
| 0182 | 0.5 | NA | NA | NA. | NON | ACTO | 4/23 |
| @ | 50% | 24 48 | 0 | 0 | MY | MSP | 4/24 |
| 0182 | 0,5 | na | NA | NA | מנו | 1 | 4/23 |
| B | 10.0% | 24 | 0 | 0 | 1130 | IIN | |
| 0/82 | 0.5 | NA | NA | · NA | w | LDN | 4/23 |
| \Box | 1.0%; | 24 | 0 | | ADO | 100 | 4124 |
| | | NA | · NA | NA. | 4 | | 77. |
| | | 48 | | : | · · · |) | |
| | | NA | XX. | NA. | | ! | |
| | | 24 | | | | 4 | |
| | | 48 | | | | | |

a - Dosage applied by technician indicated NA - Not Applicable.



Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

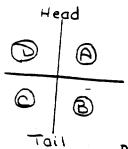
Test Group:

RT No. 8510938 Venicle Stenle 0.9% Material Unisoft 222-90
Saline LOT = SC 49-66A 64478

Date Animal Received 4/3/8/
Source Deam Daul Sex 3 Date Initiated 4/2/18

| | | | | | Tec | Rec | |
|------------------|-------------------|-------------------------------------|--------------|-------|------------|-------------|--------------|
| Animal No. Site | Dose ² | Obser- vation Period (Hrs) | Erythems | Edena | mician | Recorded By | Date |
| 0156 | 0.5 | NA | NA | NA | NOW | Se. | 4/21 |
| <u> </u> | 25% | 24 48 | 2. 0 | 1 0 | CO | M79 | |
| 0156 | 0.5 | NA | - NA | NA | 1170 | ER | 4/21 |
| <u>®</u> | 50% | - 24 - 48 | 2.0 | 2.0 | CO LIN | NOW PCN | |
| 0156 | 0.5 | NA | NA | · NA | No | EIZ | 4/21 |
| ٥ | 75% - | 24 ~48 | 2, O 2, O | 3.0 | N.20 | N.TO | -122 4/23 |
| 0156 | 0.5 | NA | NA | NA | MA | E.R. | 4/21 |
| <u></u> | 100% | 24 48 | 2.0 2.0 | 3.0 | 000 VCN | NZW NEW | 4/22 |
| | | HA | AK | NA | 140.4 | | 7. |
| • | | 24 | | | | | |

a - Dosage applied by technician indicated



Dose Ranze

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Test Group:

RT No. 856938 Venicle Sterile 0.9% Material Varisoft 222-90 Saline LOT # SC 49-100A104475

Date Animal Received Source Dean Day Date Initiated 4/2/18

| | | | | | Tec | Rec | |
|------------------------------|-------------------|-------------------------------------|--------------|-------|-----------|-------------------|-------|
| 6410 - Animal No. 5,70 | Dose ⁴ | Obser- vation Period (Hrs) | Erythema | Edema | mician | Recorded by | 1981 |
| 0119 | 0.5 | NA | NA | NA | RUN | FR | 4/21 |
| <u> </u> | 100% | 24 48 | 2,0 | 3.0 | Co | 1179 | 1/122 |
| 0119 | 0.5 | NA | NA | NA NA | RCN | | 14/23 |
| <u>(3)</u> | 25% - | . 48 | /, O 2, O | 10 | 00 | NJO | 4/21 |
| 0119 | 0.5 | NA | NA NA | . NA | NOW | L.JQ ER | 4/23 |
| 0 | 50% - | 24 48 | 2.0 | 2.0 | CO | OCLA: | 4/22 |
| 0/19 | 0.5 | NA | NA | NA. | NDA | ER | 4/21 |
| | 75% | 24 1 | 2.0 | 2.0 | Ca 150 | 14/79 Y | 1/22 |
| | | NA. | WA. | NA | FJU" | \(\frac{1}{2} \) | 1/73 |
| | | 24 | | | | | |

a - Dosage applied by technician indicated

Dose Ranze

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Test Group:

RT No. <u>R56938</u> Vehicle <u>Sterile 0.9% Material Volus of + 222</u>-90

Soline Lot = SC 49-668644750

Date Animal Received Source Dean Daul Sex 07 Date Initiated 4/2/18

| | | | | | Jec | Rec |
|------------------------------|-------------------|-------------------------------------|----------|-------|--------------|--------------------|
| 6410 - ADIMAL NO. Site | Dose ^a | Obser- vation Period (Hrs) | Erythema | Edema | lecimician . | Date 9 |
| 0143 | 0.5 | NA | NA | NA | Man | FR 4/21 |
| @ | 75% | 24 48 | 2.0 | 2.0 | GO | MX 4/12 MN 4/13 |
| 0143 | 0.5 | NA | - NA | NA | NON | se! 4/21 |
| <u>③</u> | 100% | 24 48 | 2.0 | 3.0 | (CO) | ND 4/2 |
| 0143 | 0.5 | NA | NA NA | · NA | DCN | R 4/23 |
| | 25% - | 24 48 | 7. O | 1.0 | W/N | NJ9 4/22 |
| 0/43 | 0.5 | na | na | NA | NDR | ER 4/21 |
| | 50% | 24 ! 48 i | 2.0 | 2.0 | | 1/20 1/22 |
| | | MA | NA | NA | RIS/31 | 1 1127 |
| | | 24 48 | | | | |

a - Dosage applied by technician indicated

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

| Test Group: | RT No. | 856938 | Venicle Sterile 0.9% Soline | Test Material Varisult 222-90 LOT = SC 49-66864475 |
|-------------------|--------|--------|-----------------------------|--|
| Date Animal Recei | ved | 4/3/8 | · . | |

Date Initiated 4/21/8/

Dean Daul Sex 7

| 6410 - Asimal No. | Dose ² | Obser- vacion Period (Hrs) | Erytheńs | Edema | Technician | Recorded By | Date |
|----------------------|-------------------|-------------------------------------|----------------------------|--------------------|--------------|-------------|-------|
| 0144 | 0.5 50% | MA 24 48 | NA 2.0 | NA 2.0 | NJA | EP NIM | 4/21 |
| 0144 | 0.5 | NA 24 48 | 2.0 - NA 2.0 | NA 13.0 | 100 100 | ER | 4/23 |
| 0144 | 0.5 | NA 24 48 | 3. 0 NA 2. U 2. 0 | 3, 0 NA 3, 0 | 1774 1774 | LER NA | 4/21 |
| 0144 | 0.5 25% | NA 24 1 | NA 2.0 | NA 2, C | 12X | ER | |
| | | %A 24 48 | NA. | NA | N.C. | | 4.7.5 |

a - Dosage applied by technician indicated NA - Not Applicable



Dose Ranze

| Test Group | : RT No. 8 <u>56</u> | 738 Venicle | IN GUINEA PIGS Test Storile 0.9% Material Saline LOT = SC. | V <u>arisoft 222</u> -9 49- 660 644150 |
|-------------|----------------------|-------------|--|--|
| Date Animal | 11- | 4 | | |
| Source | Deans Daul | _ Sex | Date Initiated | 4/23/81 |
| | | | | |

| | , | | | | Tech | Rec | |
|------------|-------------------|-------------------------------------|----------|-------|------------|-------------|------------------|
| Mimel No. | Dose ² | Obser- vation Period (Hrs) | Erythema | Edema | Teclmician | Recorded by | Date 1981 |
| 0129 | 0.5 | NA | NA. | NA | Ray | | |
| <u>(A)</u> | 1.0% | 24 48 | 0 | 0 | 949 | 100 | |
| 0/29 | 0.5 | na | - NA | NA. | NAO | ER | 4/23 |
| B | 5.0% | 24 -48 | 1.0 | 1.0 | mo | 37 | 4/24 |
| 0/29 | 0.5 | MA | NA | · NA | NOO | ER | 4/23 |
| (2) | 10.0%; | 24 48 | 2.0 | 1.0 | 140 P | np | 4/24 |
| | | MA | NA | NA. | | 0 | 0/12 |
| | | 48 | 1 | | | , | |
| | | NA | AK | - NA | | | |
| | | 24 48 | | | | | |

a - Dosage applied by technician indicated NA - Not Applicable

① recording error 4/23/8: EL

Head D B

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Test Group: RT No. 85/0938 Venicle Ston. Vo. 0.9% Material Varisoft. 222.90

Salve LOT # 50-49/060/044750

Date Animal Received 4/3/8/
Source Dean Daul Sex 7 Date Initiated 4/23/8/

| | | | | | Technic | Rec | L |
|-----------------------------|-------------------|-------------------------------------|-------------|------|-----------|-------------|------|
| 0410 - simal No. Site | Dose ⁴ | Obser- vation Period (Hrs) | Erythema | | nician | Recorded By | Date |
| 0183 A) | 0.5 | KA | NA | KA | NOR | NOO | 4/23 |
| <i>A</i>) | 10.0% | 24 48 | 1.0 | 1.0 | UTO TP | NTO | 4/24 |
| 0183 | 0.5 | MA | AN | NA | N/PP | NOV | 4/23 |
| B | 1.0% | 24 48 | 0 | 0 | NIPO | 157 | 4/24 |
| 0183 © | 0.5 | NA | MA | · NA | NOO | 1 | 4/23 |
| (C) | 5.0% | 24 48 | 2. O 3.0 | 2.0 | NOR | NZS | 1/24 |
| | | RA | NA | NA | | | |
| | | 24 | | | | | |
| | | NA | ŅA. | RA | | | |
| | | 24 | | | | | |

⁻ Dosage applied by technician indicated

Head Olo Tail

Dose Range

| | • | DEF | rmal sensitiza | ATION STUDY IN | GUINEA PIG | <u>ss</u> | | |
|-------------|------------------------------|-------------------|-------------------------------------|----------------|---------------------|-----------------|-------------|--------|
| \boxtimes | Test Gr | oup: Rī | r no. 8 <u>5693</u> | 8 VenicleS# | nile 0.9% Saline | Test Materia | uVar | 150f+2 |
| | | | Daul | | • | | | 4/23/8 |
| | | | | | | Tech | Rec | |
| | 6410 - Animal No. Site | Dose ² | Obser- vation Period (Hrs) | Erythema | Edema | [ecimician | Recorded By | 1981 |
| | 0182 @ | 5.0% | NA 24 48 | NA O | NA O | 128 | | 4/23 |
| j | 0182 B | 0.5 | NA 24 48 | NA O | NA | 11X 11X | NO | 4/23 |
| | 0/82 | 0.5 | NA 24 48 | MA O | NA O | 100 | NX | |
| | | | NA 24 48 | NA. | NA. | | | |
| | | | NA 24 48 | NA | NA. | | | |

a - Dosage applied by technician indicated
 NA - Not Applicable

Tail

Pose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Test Group:

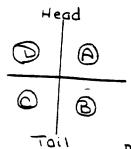
Test RT No. 85/0938 Venicle Stenle 0.9% Material Unisoft 222-90 Soline LOT = SC 49-668 64475

Saline

Date Animal Received _ 4/3/81 Date Initiated 4/2/18

| | • | | <u></u> | Ţ | Tecin | Reco | 2 |
|-------------------|-------------------|-------------------------------------|----------|-------|-----------|-------------|-----------|
| Latinal No. Site | Dose ² | Obser- vation Period (Hrs) | Erythema | Edema | ecimician | Recorded By | Date 1981 |
| 0156 | 0.5 | NA | na. | NA | NOR | re | 4/21 |
| <u> </u> | 25% | 24 48 | 2.0 | 0 | Co | 1279 | |
| 0156 | 0.5 | MA | NA | NA | 1670 | ER | 4/21 |
| B | 50% H | 24 48 | 2.0 | 2.0 | CO N.M | | 4/22 |
| 0156 | 0.5 | NA | NA | · NA | Mo | EIZ | -4/21 |
| ٥ | 75% - | 24 48 | 2,0 | 3.0 | N.30 | NJ79 | |
| 0156 | 0.5 | NA | NA | NA | IDA | E.R. | 4/21 |
| <u></u> | 100% | 24 48 | 2.0 | 3.0 | CC11 | NIN | 4/22 |
| | | - RA | MA. | NA | | | |
| | | 24 48 | | | | | |

a - Dosage applied by technician indicated -



Dose Ratiza

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Test Group:

RT No. 856938 Venicle Sterile 0.9% Material Varisht 222-9
Saline Lot #SC 49-6686447

Date Animal Received 4/3/8/
Source Dean Daul Sex 7

Date Initiated 4/2/18

| | | | | | [ec] | Rec | |
|------------------------------|-------------------|-------------------------------------|------------|----------------|------------|-------------|-------|
| 6410 - Animal No. Site | Dose ² | Obser- vation Period (Hrs) | Erythema | Edema | Technician | Recorded by | 1981 |
| 0119 | 0.5 | NA | na | NA. | NIR | ER | 4/21 |
| A | 100% | 24 48 | 2.0 | 3.0 | CO | | 4/22 |
| 0119 | 0.5 | NA | NA | NA | KU | ER | 14/21 |
| <u>(3)</u> | 25% | . 48 | /, O | 1.0 | NJA | DCM. | 4/23 |
| 0119 | 0.5 | NA | NA | · NA | NOW | ER | .4/21 |
| 0 | 50% | 24 48 | 2.0 2.0 | 1 3.0 | 1137 | NTO | 4/22 |
| 0/19 | 0.5 | NA | NA | NA | NDA | ER | 4/21 |
| | 75% | 24 48 | 2.0 | · 2.0 · 3.0 | 1/20 | 1117 | 1/23 |
| | | NA | NA. | NA | | ! | |
| | | 24 48 | | | | | |

a - Dosage applied by technician indicated

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Test Group:

Vanicle Sterile 0.9% Material Volus of + 222-90
Saline LOT = SC +9-668644750 RT No. <u>256938</u>

413181 Date Animal Received _ Date Initiated 4/2/18

| · | | | | | Tecly | Rece | 2 |
|------------------------------|-------------------|-------------------------------------|----------|-------|------------|--------------|----------|
| 6410 - animal No. 517e | Dose ² | Obser- vacion Period (Hrs) | Erythema | Edens | nician | Recorded by | 1981 |
| 0143 | 0.5 | KA | KA | RA | NDX | ER | |
| @ | 75% | 24 48 | 2.0 | 3.0 | GO LUTA | MN | 4/13 |
| 014.3 | 0.5 | KA | NA | NA | NOA | 58 | 15/4 |
| 3 | 100% | 24 48 | 2.0 | 3.0 | 100 | IN TO | 4/23 |
| 0143 | 0.5 | NA. | MA | · KA | NOO | ER | 4/21 |
| 0 | 25% | 24 48 | 3.0 | 1.0 | NLA | : 11X | 4/22 |
| 0/43 | 0.5 | NA | NA | NA | M | l ER | 1/21 |
| | 50% | 24 48 | 2.0 | 2.0 | 120 | INDA INTA | 4/22 |
| | | WA- | YA. | NA. | | <u> </u> | |
| | | 24 48 | | | | | |

a - Dosage applied by technician indicated

Dose Range

Dean Daul Sex 7

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

| | | | TOTAL TION |
|----------------------|-------|---------|--|
| Test Group: R | I No. | 8569.38 | Venicle Sterile 0.9% Material Varisult 222-9 Soline Lot # SC 49-668644 |
| Date Animal Received | d | 4/3/8 | • |

Date Initiated 4/21/8/

| | , | | | — — | Tecl | Reco | <u> </u> |
|-----------------------------|-------------------|-------------------------------------|--------------|----------------|------------|-------------|----------|
| 6410- animal No. Site | Dose ⁴ | Obser- vation Period (Hrs) | Erythema | Edema | nician | Recorded By | 1981 |
| 0144 | 0.5 | KA | NA | NA | MCN | 52 | 4/21 |
| | 50% | 24 48 | 2.0 | 3.0 | 00 | INTIA | |
| 0144 | 0.5 | MA | NA | NA | NON | ER | 4/21 |
| <u> </u> | 75% | 24 48 | 2. O | 13.0 13.0 | 131 131 | NLX | 4/22 |
| 0144 | 0.5 | NA | NA | NA. | MA | ER | 4/21 |
| | 100% | 24 48 | 2. U 2. O | 3, 0 3, 0 | | N7Q | 1/22 |
| 0144 | 0.5 | NA | KA | NA | KOK | ER | 4/21 |
| | 25% | 24 i | 2. O 2. O | . 2.0 | | 1170 | 4/22 |
| | | NA. | AN. | NA | | | |
| | | 24 48 | | | | | |

a - Dosage applied by technician indicated

JUN 1 9 1981

Other Raitech Scientific Services Laboratories: St. Louis MO Gray Summit MO

P.O. Box 7545 • Medison, Wisconsin 53707 • 606/241-4471

A Division of Raiston Purina Company

GUINEA PIG MAXIMIZATION STUDY OF VARISOFT 222-90 LOT #SC49-66B 644750

SPONSOR:

SHEREX CHEMICAL CO.

DUBLIN, OHIO

STUDY NO. 856939

INITIATION: 4/27/81

COMPLETION: 5/21/81

REPORTED:

6/3/81

SAMPLE:

VARISOFT 222490 LOT #SC49-66B 644750

ENCLOSED:

METHOD, PAGES 2 AND 3

SUMMARY, PAGE 4 RAW DATA APPENDIX

SIGNED:

Hanry G. alinechit

TECHNICAL SUPERVISOR

GARY W! THOMPSON, BS

MANAGER, ACUTE TOXICOLOGY

STUDY DIRECTOR

BY AND FOR RALTECH SCIENTIFIC SERVICES

RAW DATA FOR THIS STUDY IS KEPT ON FILE AT RALTECH SCIENTIFIC SERVICES, MADISON, WISCONSIN.

Reports are submitted to clients on a confidential base. No reference to the work, the results or to Reltach Scientific Services in any form of advertising, news release or other public ennouncement may be made without written authorization from Releast Scientific Services.

Test Material: Varisoft 222-90 Lot #SC49-66B 644750

Test Animal: Young adult male guinea pigs were procured, maintained individually in stainless steel cages in temperature and humidity controlled rooms, provided continuous access to Purina Guinea Pig Chow and water and held for an acclimation period of at least 7 days.

Test System: Ten male guinea pigs weighing between 426 and 500 grams were chosen at random and used for this study. The animals were individually housed and identified by animal number and ear tag.

Preparation of Test Material: For the intradermal injections the Freund's Complete Adjuvant Solution was prepared by adding 5 mL of sterile water for injection in 1 mL increments to 5 mL of Freund's Adjuvant.

The 5% solution of test material in sterile water was prepared by taking 0.25 gram of Varisoft 222-90 Lot #SC49-66B 644750 and adding sterile water for injection to a total volume of 5.0 mL.

The 5% solution of test material in Freund's Adjuvant was prepared by dissolving 0.25 gram of Varisoft 222-90 Lot #SC49-66B 644750 in 2.5 mL of sterile water and adding 2.5 mL of Freund's Adjuvant in 1 mL increments to a total volume of 5.0 mL

For the topical induction and challenge procedures the Varisoft 222-90 Lot #SC49-66B 644750 was applied at 10% w/v and 1.0% w/v suspensions in 0.9% saline, respectively.

Method: A 4.0 x 6.0 cm area was clipped along the midline over the shoulder region. Two rows of three-deep intradermal injections (total of 6 injections) were made within the boundaries of a 2.0 x 4.0 cm area, one row on each side of the midline as follows: 0.05 mL of the prepared Freund's Adjuvant Solution, 0.05 mL of a 5% aqueous test solution, and 0.05 mL of a 5% solution of test material and Freund's Adjuvant Solution.

One week after the injections, the same area was clipped and closely shaved with an electric razor. A 2.0 x 4.0 cm patch of Whatman No. 3 filter paper was saturated with a 10% w/v suspension of Varisoft 222-90 in 0.9% saline, placed over the injection sites, then covered with an overlapping of Blenderm tape and secured by an overwrap of Elastoplast tape. The dressing remained in place for 48 hours.

Two weeks after topical induction the animals received a challenge dose. The hair was removed from a $5.0 \times 5.0 \text{ cm}$ area on the flank by clipping and

shaving as before. A 1.0% w/v suspension of test material in 0.9% saline was applied on a 2.0 x 2.0 cm piece of filter paper in the same fashion as for topical induction. The patch was sealed to the flank for 24 hours under a 4.0 cm strip of Blenderm tape. Complete occlusion was made by an overwrap with Elastoplast tape wound around the trunk.

Observations: Twenty-four hours following patch removal the test sites were examined for erythema and edema. The sites were examined again at 48 hours after patch removal to detect weak, slowly developing reactions. The test sites were shaved 3 hours prior to the 24 hour reading. The reactions were scored according to the following 4-point scale:

- 0 = no reaction
- 1 = scattered mild reduess
- 2 = moderate and diffuse redness
- 3 = intense redness and swelling

The important statistic in maximization testing is the frequency of sensitization, not the intensity.

Test Animal: Albino guinea pigs Source: Dean Daul, Luxemburg, WI Date Animals Received: 4/10/81

Test Material: Varisoft 222-90 Lot #SC49-66B 644750

Date Test Started: 4/27/81 Date Test Completed: 5/21/81

| Anim ä l Number | Sex | 24 Hours Right | 48 Hours |
|---------------------------|-----|-------------------|----------|
| | | | Right |
| 64100226 | M | 0 | 0 |
| 64100227 | М | 1 | 1 |
| 64100228 | M | 1 | 1 |
| 64100229 | M M | <u> </u> | 0 |
| 64100230 | | <u> </u> | 1 |
| | M | 1 | 1 |
| 64100231 | M | 1 | Ō |
| 64100232 | M | <u> </u> | |
| · · | | 0 | 0 |
| 64100233 | M | 0 | 0 |
| 64100234 | M | 0 | Ö |
| 64100235 | ¥ | 0 | U |
| 04100233 | M | 0 | 0 |

General Behavior and Appearance:

All of the guinea pigs used in this study appeared normal throughout the study period. Normal body weight gains were recorded for seven animals during the course of the study. One animal (No. 64100234) exhibited a body weight loss, one animal showed no gain in body weight and one animal exhibited a slight body weight gain during the second week on test. These animals had normal body weight gains during the third week on test.

Skin Reactions to Varisoft 222-90 Lot #SC49-66B 644750:

Five animals exhibited a sensitization reaction to the test material following the challenge application. Each animal reacting to the challenge dose exhibited a mild redness at 24 hours and three of these animals continued to show a mild redness at the 48 hour observation. The other five animals did not exhibit any reaction to the challenge dose at either the 24 or 48 hour observations.

Conclusion:

Based upon the results obtained, the test material, Varisoft 222-90 Lot #SC49-66B 644750, is considered a skin sensitizer in guinea pigs.

Reference:

Magnusson, B. MD, and A. Kligman, PhD, MD, Allergic Contact Dermatitis in the Guinea Pig, Charles C. Thomas, pub., 1970, pp. 113-117.

GUINEA PIG MAXIMIZATION TEST

| Test Compound Varia | soft 222-90 L | ot #5c 49-66 | B - RT No. <u>85</u> | 6939 |
|-----------------------|------------------|--------------|----------------------|-----------|
| | | 6 9 9 7 5 3 | _ Sponsor No. | |
| Date Animals Received | 4/10/81 | | | lean Daw |
| Date of Intradermal I | njections $4/27$ | 181 | | SW, M, NJ |
| Date of Topical Appli | | | Technician | • |
| Date of Challenge | | | | \sim |
| | | | Technician | MIN ER |
| | 24 Hour | 3 | 48 Hou | rs |
| Animal No., Sex | Right | Left | Right | Left |
| 6410-0226 0 | 0 | | 0 | \ |
| 0227 0 | | | . , | |
| 0228 0 | | | 0 | |
| 0229 0 | | | 1 | |
| 0230 | | | , | |
| 0231 07 | | | 0 | |
| 0232 07 | 0 | | 0 | _ ` |
| 0233 07 | 0 | | 0 | |
| 0234 07 | 0 | | 0 | |
| 0235 07 | 0 | | 0 4 | \$ 1. All |
| Technician | Co | , | SP | |
| Recorded By | ER | | F | |
| Date /98/ | 5/20 | | Shi | |

Scoring Code: 0 = Normal, No Reaction

1 = Scattered Mild Redness

2 = Moderate and Diffuse Redness

3 = Intense Redness and Swelling

| REVIEWED | BY: | - N. | DATE: 52918 |
|----------|-----|------|-------------|
|----------|-----|------|-------------|

OMaximization Dermal Sensitization In Guinea Pigs - Body Weights

| X | _ | _ | | |
|---|--------------|----------------------|------------|----------------|
| Щ | Test Group | RT No. <u>856939</u> | Vehicle NA | - |
| | | | | · INTIGOTE AAA |
| | Positive Cor | atrol Group NA | Vehicle NA | Lot #50 49-66B |
| | - | | | 644750 |

| | T | , | Animal | Number | | | | 7 | |
|-------|----------|--|-------------|--------|-------|-------|------------|-----------------|--------------|
| 6410- | 6410- | 6410- | 6410- | 6410- | 6410- | 6410- | 6410- | | 1651 |
| 0226 | 0227 | 0228 | 0229 | 0230 | 0231 | 0232 | 0233 | Tech- nician | 1981 Date |
| 450 | 500 | 456 | 482 | 447 | 426 | 464 | 497 | | 1/1 |
| 5/4 | <u> </u> | 516 | 532 | 483 | 481 | 5/8 | 559 | Sw yy | 4/27 |
| 536 | 686 | 540 | <i>55</i> 3 | 496 | 481 | 547 | | | 5/4 |
| 633 | J81 | 633 | 600. | 583 | 595 | 621 | 566 C62 | duk | 5/11 |
| | | | | | | | 202 | JP NOW | 5/18 |
| | | | | | | | | | |

| | | Animal Number | | |
|-------|-------|--------------------------|-----------------|--------------|
| 6410- | 6410- | · | | |
| 0234 | 0235 | | Tech- nician | 1981 Date |
| 468 | 495 | Scale Used: K-Tron 4809 | | |
| 518 | 583 | Scale Used: X.Tron 4809 | <u> </u> | 4/27 |
| 405 | 437 | Scale Used: K-Tron 4809 | Jup - | 5/4 |
| 5/2-1 | 722 | Scale Used: K-TRON -1809 | N 170 | 5/11 |
| , | | Scale Used: | JP 100 | 5718 |
| | | Scale Used: | | |

O Form Change 5w 4/27/81
NA - Not Applicable

Head المنا

Dose Range DERMAL SENSITIZATION STUDY

| Test Gr | oup: | No.85169 | 79 VehicleS | terse 0.9, Salve | . <u>GS</u> Test Mater: LO7 | ial Va | 1 VI SOL |
|-------------------------------|-------------------|-------------------------------------|-------------|---------------------|--------------------------------------|-------------|-------------|
| Date Ani | mal Receive | d 4/3/ Daul | 81 | • | Initia: | | 4123/8 |
| 0410 - ADIBAL No. Site. | Dose ^a | Obser- vation Period (Hrs) | Erythema | Edema | <u> Technician</u> | Recorded by | Pate (0.87) |
| 0186 | 0.5 | NA 24 | NA O | NA | NOV | NOS | 4/23 |
| | 1.0% | 48 | Ü | | ACTO | 157 | 4/24 |
| 0186 | 0.5 | NA | NA | NA. | PEN | אנא | 4/23 |
| (B) | 5.0% | 24 | | 0 | 100) 100) | ALN | <u> </u> |
| 0186 | 0.5 | NA | NA NA | · NA | 100 | SP | 4/23 |
| | 10.0% | 24 | 2.0 | 1.0 | W | 1179 | 4/24 |
| | | KA 24 | 2.0 NA | N.4 | € P | JP | 4/25 |
| | | 48 | | : | | ; ·- | |
| | | NA | AV | | | | |

a - Dosage applied by technician indicated
 NA - Not Applicable

Wead D Ta.1

Dose Ramas

| | DI | RMAL SENSITIZ | ATION STUDY II | N GUINEA PI | :GS | | |
|------------------------------|-------------------|-------------------------------------|----------------|-------------|----------------|-------------|----------|
| Test Gr | oup: [| RT No. 8569 | ATION STUDY II | Sale 09 | Test Mater: | ial V | <u> </u> |
| Date Ani | mal Receive | 2 4/3/0 Daul | 91 | • | | | 4/23/ |
| | 7 | | | | Tecl | Rec | |
| CO410- Animal No. SiTe | Dose ² | Obser- vacion Period (Hrs) | Erythema | Ed ema | [eclmician | Recorded By | 1981 |
| 0187 | 0.5 | NA 24 | NA | NA | Par | Pan | |
| \bigcirc | 10.0% | 48 | 2.0 | 1.0 | SEN. | MN | 4/21 |
| 0187 | 05 | NA | AK | NA. | NOO | NOO | 4/23 |
| \mathcal{B} | 1.0% | · 48 | <u> ၁</u> | 0 | NO | NO | 4/24 |
| 0/87 | 0.5 | NA | NA | . NA | NDO | 100 | 4/23 |
| | 5.0% F | 24 | 1.0 | 1 1.0 | | DXI | 4/24 |
| | | NA | NA NA | I/O | | - | 4/85 |
| - | | 24 | | i | | | |
| | | | | : | | i | <u> </u> |

a - Dosage applied by technician indicated
 NA - Not Applicable

24 48

Dose Ratice

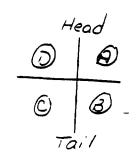
DERMAL SENSITIZATION STUDY IN GUINEA PIGS

RT No 85/8/39 Venicle Stanle 0.9% Material Varisoft 222-90
Saline LOT 750-49-668644750 est Group:

te Animal Received 4/3/8/ Date Initiated 4/33/87

| | | | | | [ec] | Rec | |
|-------------|-------------------|-------------------------------------|----------|-------|--------|-------------|----------|
| 0 21 No. | Dose ² | Obser- vation Period (Hrs) | Erythema | Edema | mician | Recorded by | 181 -181 |
| £8 | 0.5 | NA | NA | NA | NTO | PUN | 4/23 |
| (8) | 5.0% | 24 48 | 1.0 | 0 | NN | 101 | :4/24 |
| -0 | 0.5 | MA | NA | NA | w | NDV | 4/23 |
| | 10.070 - | 24 48 | 2.0 | 1.0 | 100 | 1/8 | 4/24 |
| 8 | 0,5 | NA | NA | · NA | NJA | DOCU | 1 |
|) | 1.0% - | 24 48 | 0 | 0 | NY | 1120 | 4/24 |
| | | KA | NA | NA | | | 1,2 |
| | | 24 1 | | : | | i | • |
| | | MA | MA | HA | | | |
| • | | 24 48 | | - | | | |

Dosage applied by technician indicated Not Applicable



Cose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Test Group: Venicle Sterile 09% Material Varisoft 222-90 Saline Lot No. SC 49-6686447 RT No. 856939

Date Animal Received Source Deans Doul Date Initiated 4/21/8

| 6410- Animal No. 5, te | Dose ¹ | Obser- vation Period (Hrs) | Erythema | Edema | <u>Ceclmician</u> | Recorded by | Date |
|------------------------------|-------------------|-------------------------------------|--------------------|--------------|-------------------|----------------------|--------------|
| 0161 A | 0.5 25% | NA 24 48 | NA 1. O | NA O | NJV | 1 F.R. | 4/2 |
| 0161 | 0.5 | NA 24 48 | 2. 0 NA 2. 0 | NA 1.0 | NO0 NOX Co | 1000 1000 1000 | 4/21 |
| 0161 O | 0.5 75% - | NA 24 48 | 2. 0 NA 2. 0 | 2. 0 • NA | | 23 201 | 4/21 |
| 0161 | 0.6 | NA 24 1 | NA 2. 0 3. 0 | RA NA | NDR | SE ALXO | 4/23 4/23 |
| | | NA 24 48 | AN. | S.O | NOO | 1001 | 1153 |

a - Dosage applied by technician indicated

NA - Not Applicable

| <u>6</u> | @ |
|----------|----------|
| © | 3 |

Dose Ranze

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

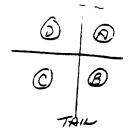
Test Group:

RT No. 8510939 Venicle Sterike 0.9% Material Varisof 1 222-90 Saline Lot No. SC 49-668644

Date Animal Received 4/3/81 Source Dean Daul Date Initiated 4/2/18

| 640 Louisel No. Site | Dose ² | Obser- vation Period (Hrs) | Erythema | Edema | <u>Tecimician</u> | Recorded by | Date |
|----------------------------|-------------------|-------------------------------------|------------------|------------|-------------------|-------------|------|
| 0162 | 0.5 | NA 24 | NA | NA 3. G | NOD | 66 | 1981 |
| 0162 | 0.5 | 48 NA | 2, O NA | 3.0 | N3X | 1000 | 4/23 |
| 0162 | 2570 | 48 | 2.0 | 1.0 | 1730 | 1120 | 4/32 |
| © | 0.5 507° - | NA 24 48 | NA 2.0 2.0 | 3. O | NOO | FR | 4/21 |
| 0,165 | 0.5 | RA 24 | Na | NA NA | NON | 1720 | 4/21 |
| | 75% | 48 | 2.0 2.0 | 3.0 | 100 | 1000 I | 4122 |
| | | #A 24 48 | NA. | NA | | ! | |

a - Dosage applied by technician indicated

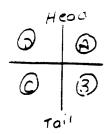


Dose Range Dermal Sensitization Study in Guinea Pigs

| Test Group: | RT No. <u>85/0939</u> Veni | cleSterile 0.97 Material Varisof Saline LOT NO. SC 49. | <u>†</u> 272-4 |
|-------------|----------------------------|---|----------------|
| | eived 4/3/8/ | | |
| Source Dear | ne Doul Sex _ | Date Initiated 4/21/ | 81 |

| | 1 | | | | [ec] | Rec | |
|------------|------------------------|-------------------------------------|--------------|-------|--------|-------------|--------|
| Animal No. | Dose ² (ml) | Obser- vation Period (Hrs) | Erythema | Edema | nician | Recorded By | Date |
| 0164 | 0.5 | MA | NA | NA | NJX | | 1981 |
| <u>(A)</u> | 75% | 24 48 | 3.0 3.6 | 3,0 | CO | INJX | : 4/22 |
| 0164 | 0.5 | NA | NA | NA NA | NDO | NTO | 4123 |
| B | 100 % | 24 | 2.0 3.0 | 13.0 | co | 1 EE | |
| 0164 | 0.5 | NA | NA | · NA | NOS | | 4173 |
| | 25% | 24 | 7. O 2. O | 4.0 | CO | LON | 4/22 |
| 0104 | 0.5 | NA | NA | NA | NON | 1 20 | 1173 |
| | 50% | 24 | 2.0 | 1.0 | N23 | SE NTR | 4/21 |
| | | MA | NA | NA | W. 7 | 100 | 4123 |
| | | 24 | | | | | |

a - Dosage applied by technician indicated NA. - Not Applicable



Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS est Group:

Venicle Ster. le 0.9% Material Varisof + 222-90
Soline LOT NO. SC-49-68644750

te Animal Received _ 413/81 Date Initiated 4/2/18

| al No. | Dose ⁴ (m1) | Obser- vation Period (Hrs) | Erytheme | Edena | Technician | Recorded by | Pate |
|----------------|------------------------|-------------------------------------|--------------|-------|------------|---------------|-------------|
| <i>o3</i> ∋ | 0.5 | NA | MA | NA | XLN | ER | 4/21 |
| <u> </u> | 50% | 24 48 | 2.0 3.0 | 2.0 | co | ADO | : 4/22 |
| 0. | 0.5 | NA | NA | NA | NOW | 100 | 4123 |
| <u>3</u> 93 | 75% | 24 48 | 2.0 | 3. a | co | 12 T | |
| 3ء | 0.5 | NA | NA | · NA | NON | i son | 4123 |
| | 1007. | 24 | 2.0 | 30 | 30 | MOS | 4/22 |
| 63 | 0.5 | NA | NA · | NA | NO OCT | NEO | 4123 |
| j | 25% | 24 ! 48 j | 2. o 3. o | 2.0 | 00 | NOX) | 4/21 |
| | | MA | NA | NA | 100 | 0 0 100 | 4/53. |
| | | 24 | | | | | |

Dosage applied by technician indicated Not Applicable according error 4/21/81 ER

Head Tail

Dose Range

| Test Gr | oup: | RT No.8 <u>5/09</u> - | ATION STUDY I | N GUINEA ? | Test Mater: LO7 | ial V | 141504 49668 |
|-------------|----------|-----------------------|------------------|------------|-----------------------|----------------|-----------------|
| | | Daul | | Date | Initia | ted . | 4123/8 |
| | | | | | | _ | 4/43/X |
| | | • | | | ie | 75 | _ |
| 0410- | | a | | T T | Technician | Recorded | Date |
| AD imal No. | 4 | Obser- vation | Erythema | Edema | cla | ded | e e |
| Site. | (m1) | Period (Hrs) | | | | B y | |
| 0186 B | 0.5 | KA | *** | | 1.00 | 1 | 1987 |
| | 1.0% | 24 | NA O | NA NA | NO | NOS | |
| | 7.076 | 48 | U | 1 0 | 1 12 | 157 | 4/24 |
| 0186 | 0.5 | na | NA | FA | PEN | 1 | 1 |
| B | = 07 | 24 | 0 | 1 0 | | INDS | |
| | 5.0% | . 48 | 0 | | 100 | 1/3 | 4/24 |
| 0186 | 0.5 | NA | | | ĺ | ادمو | i i |
| | 10.0% | 24 | NA 2.0 | NA. | 1000 | NON | 4/23 |
| | 10.0 101 | 48 | 20 | 1.0 | 1000 OP | MM | 4/24 |
| | | | | <u> </u> | | 1 | 4/25 |
| <u> </u> | | NA I | NA. | N.A. | • | ļ | ſ |
| ! | <u> </u> | 26 | | i | | 1 \ 1 | |
| 1 | | 48 | | : | | i l | |
| | | MA | MA | | | ! | |
| Γ | | 24 | | 1:1 | | | |
| | | 48 | | | | | |

a - Dosage applied by technician indicated NA - Not Applicable

Wead) Tail

Dose Range

| | Ī | ERMAL SENSITI | ZATION STUDY I | N GUINEA E | TCC | | |
|------------|-------------|---------------|----------------|------------|---------------|-----------------|-------------|
| Test | Group: | RT No. 856 | 239 Venicle | Sterle O. | Test Mater | ial \ | brien |
| | | | • | Saline | . 207 | + 50 | 40-14 |
| Date An | imal Receiv | ا د/4 | d | • | | | 11-00 |
| | 2 | ed 4/3/ | 7 | | | | |
| Source . | Dear | 1 Daul | Sex | Date | Initia | ted | 4/23/ |
| | | | | | | - | |
| | | | | | = | | |
| C0410- | 1 | | | | ec | Rec | |
| ! | | Obser- | | | mician | Recorded | <u>Date</u> |
| Animal No. | | Vation | Erythema | Edema | | led | ro . |
| Site | (nil) | Period (Hrs) | | | - | 87 | |
| 0187 | 0.5 | | | | | | 1981 |
| | 0.5 | NA NA | NA | NA | Pal | NDO | 4/23 |
| (A) | 10.0% | 24 48 | 2.0 | 1.0 | N. TO | INN | 1123 |
| 0187 | 0.5 | | 2.0 | 1.0 | 1000 | JP | 4/25 |
| B | | NA 24 | NA | NA | NOO | ADO | 4/23 |
| 0 | 1.0% | 48 | <u></u> | 0 | INO | NO9 | 4/24 |
| 0187 | 0.5 | | | 0 | R | R | 4/25 |
| 0/87 | | NA 24 | NA NA | NA. | NOO | PON | 4/23 |
| | 5.0% | 48 | 1.0 | 1.0 | ACK | DX | 4/24 |
| | | | 1.0 | | R | 1 | 4/20 |
| | | NA 24 | NA | NA NA | • | | |
| | | 48 | | | | ``` | |
| | | | | <u> </u> | İ | | |
| | | NA 24 | NA | TEA. | | | |
| | | 48 | | | | | |

a - Dosage applied by technician indicated
 NA - Not Applicable

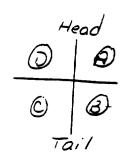
Dose Range DERMAL SENSITIZATION STUDY IN GUINEA PIGS

| Test Group: | RT No 85/8/39 V | enicle Staule 0.9% Materia | Waring (122 |
|-------------|----------------------------------|----------------------------|-------------|
| | | Saline LOTA | 5C-49-66864 |
| | ived <u>4/3/8/</u> in Daul Sex _ | Date Initiates | 4 4/32/01 |

Date Initiated 4/33/87

| Site | Dose ² (mi) | Obser- vation Period (Hrs) | Erythema | Edena | Ceclm1c1an | Recorded by | 181 |
|-------------|------------------------|-------------------------------------|-------------|---------|-------------------|--------------|------|
| 0188 (2) | 0.5 5.0% - | NA 24 48 | NA /·O | NA O | N.79 N.70 | مريم مريم | 4/23 |
| 0188 B | 0.5 | NA 24 48 | NA () (2.0) | NA V. C | 100 100 100 | NY | 4/23 |
| 0188 0 | 0.5 | NA 24 48 | NA O | /. O | DEU DEU | 1120 | 4/23 |
| | | NA | NA. | NA NA | <i>`</i> ., | 1 | 4/25 |
| | | MA 24 | MA | KA | | | • |

a - Dosage applied by technician indicated NA - Not Applicable



Dose Range

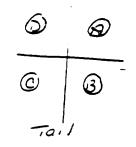
DERMAL SENSITIZATION STUDY IN GUINEA PIGS

| | SITIZATIO | N STUDY IN GUINEA PI | <u>IGS</u> |
|------------------|----------------|----------------------|------------------------------|
| Test Group: | RT No. 8516939 | Venicle Sterile 19 | Test Material Varisof+ 222- |
| | , <i>•</i> | Saline | LOT NO. SC 49-66864 |
| Date Animal Rece | ived 4/2/01 | • | |

Date Animal Received 4/3/81 Source Dean Doul Sex of Date Initiated 4/21/8

| 6410- Animal No. 5, te | Dose ² (mi) | Obser- vation Period (Ars) | Erythema | Edema | <u>[ec]nician</u> | Recorded by | Date |
|------------------------------|---------------------------|-------------------------------------|--------------|---------|-------------------|-------------|-------|
| 0161 A | 0.5 | NA | NA | 74 | 1 | | 198 |
| (D) | 25% | 24 48 | 1.0 | NA O | 100 | I FR | 4/2 |
| 0161 | 0.5 | NA | 2.0 | 1.0 | 1720 | Nu | 4173 |
| <u>B</u> | 50% | 24 | NA 2.0 | 1 /· O | 20 | 117W | 4/21 |
| 0161 | 0.5 | 48 | 2. 0 | 2.0 | NON | NOO | 4/2= |
| 0 | 75% - | NA 24 | NA 2.0 | . NA | NOO | ER | -4/21 |
| ΔU_{eff} | | 4.8 | 2.0 | 3.0 | NS0 | 100 | 403 |
| 0161 | 0.6 | · NA | NA | NA | NOO | .22 | |
| | 100% | 24 1 | 2. O 3. O | 3.0 | Co | ADO | 4/23 |
| | | NA. | AK. | | NOO | 1201 | 7153 |
| | | 24 | W. | NA | <u>:</u> | | |

a - Dosage applied by technician indicated NA - Not Applicable



Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

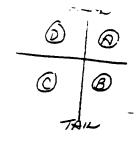
Test Group:

RT No. 85/0939 Venicle Sterike 0.97 Material Vorisod 1 222-90 LOT NO. SC 49-668644 Saline

Date Animal Received 4/3/8 Source Dean Daul Date Initiated 4/2/18

| LOHIO LOTEL No. | Dose ² (mi) | Obser- vation Period (Hrs) | Erythese | Edema | echnician | Recorded by | Date |
|--------------------|------------------------|-------------------------------------|--------------------|-----------|-----------|--|--------|
| 0162 | 0.5 | NA 24 | NA 2.0 | NA 3 G | NOD | P. P. P. P. P. P. P. P. P. P. P. P. P. P | 198 |
| 0162 B | 0.5 | NA 24 48 | 2.0 NA 2.0 | NA NA | NON | PR | 1 4/21 |
| 0162 | 0.5 | NA 24 48 | 2. 0 NA 2. 0 | . NA | VDS | FR | |
| 0,195 | 75% | NA 24 48 | 2.0 NA 2.0 | 2.0 | NDO | 1376 68 | 4/21 |
| | | 24 48 | 2.0 NA | NA NA | | 11-76 | 4128 |

a - Dosage applied by technician indicated NA - Not Applicable



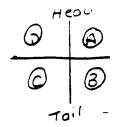
Dose Ranze DERMAL SENSITIZATION STUDY IN GUINEA PIGS

| Test Group: | STUDY IN GUINEA PIGS |
|-------------|--|
| Test Group: | RT No. 85/0939 Vehicle Sterile 0.97 Material Vari Soft 272 |
| | venicle Sier, le U.9 / Material Vorision Con |
| | Saline LOT NO. SC 49.14.81 |
| • | |

Date Animal Received 4/3/81 Source Dean Dout Sex 7 Date Initiated 4/2/1/81

| LOUID - ADIMAL NO. SITE | Dose ² | Obser- vacion Period (Hrs) | Erythema | Edema | echnician | Recorded By | Date |
|-------------------------------|-------------------|-------------------------------------|------------|-------|-----------|-------------|-------|
| 0164 | 0.5 | NA | | | 1.120 | | 198 |
| (A) | 7570 | 24 48 | NA 2.0 | J. O | NJX | EP | |
| 0164 | 0.5 | | 3.6 | 3.0 | 1.70 | NTO NTO | 1 4/2 |
| \odot | 100 % | NA 24 | 2. O | 12.0 | NON | EP | 14/2 |
| 2164 | 0.5 | . 48 | 3.0 | 3.0 | ism | N.X.) | 4/25 |
| | 25% - | NA 24 | NA /. O | · NA | NON | ! ER | 4/21 |
| 14010 | | 48 | 2.0 | 4.0 | NOO | 100 | 4/33 |
| | 0.5 | NA | NA | NA | NDO | 1140 | 4173 |
| | 50% | 24 | 2.0 | 1.0 | Co | FR | 4/21 |
| | | | 2.0 | | | NEW | 4/23 |
| | | 24 | NA | NA | | | 7.16 |
| | | 48 | | | : | | |

a - Dosage applied by technician indicated NA .- Not Applicable



Dose Ramae

| Test Group: | RT No. 85/4939 | | Test | Vanisary and Ga |
|-----------------|----------------|-------|----------------|-----------------|
| | | | Saline Lot No. | SC49-6864475C |
| Date Animal Rec | eived 413/81 | | • | |
| Source Deal | Daul se | x _ ~ | Date Initiated | 4/21/81 |

| Animal No. | Dose ^a | Obser- vation Period (Hrs) | Erythema | Edema | Tecimician | Recorded by | Date 9 |
|------------|-------------------|-------------------------------------|----------|--------------|------------|-----------------|--------|
| 0163 | 0.5 | MA | NA | NA | &W | ER | 4/21 |
| @ | 50% | 24 | 2.0 | 7.0 | co | | 1/22 |
| | 5078 | 48 | 3.0 | 12.0 | NDA | indo | 4123 |
| 0163 | 0.5 | МA | NA | NA | NOW | 58. | 4/21 |
| (B) | - 0 | 24 | 20 | 1 3.0 | 100 | TIN | |
| | 75% | 48 | 2.0 | 1 3.0 | m | NOO | 4123 |
| 0163 | 0.5 | AH | MA | · NA | NOX | į 6 0 | 4/21 |
| | 1007. | 24 | 2.0 | i 5 0 | NIN | : MÒQ | 4/22 |
| | 100 /0 | 48 | 2. 0 | 3.0 | MA | 100 | 1453 |
| 0163 | 0.5 | . NA | NA · | NA | DCI | FP | 4/21 |
| (6) | 000 | 24 | 2.0 | 11.0 | 1 (10 | ATX | 4/22 |
| | 25% | 48 | 2.0 | . 2.0 | 100 | 1130 | 4\23 |
| | | MA . | XA | NA. | | 08 | · |
| | İ | 24 | | | | 1 | |
| | | 48 | | | | | |

a - Dosage applied by technician indicated

NA - Not Applicable

Oracording error 4|21/81 ER



P.O. Box 7545 • Madison, Wisconsin 53707 • 608/241-4471 A Division of Raiston Purina Company

GUINEA PIG MAXIMIZATION STUDY OF VARISOFT 222-90 LOT #SC49-68 644750

SPONSOR:

SHEREX CHEMICAL CO.

DUBLIN, OHIO

STUDY NO. 856940

INITIATION: 4/27/81

COMPLETION: 5/21/81

REPORTED: 6/03/81

SAMPLE:

VARISOFT 222-90 LOT #SC49-68 644750

ENCLOSED: METHOD, PAGES 2 AND 3

SUMMARY, PAGE 4 RAW DATA APPENDIX

SIGNED:

TECHNICAL SUPERVISOR

GARY W. THOMPSON, BS

MANAGER, ACUTE TOXICOLOGY

STUDY DIRECTOR

BY AND FOR RALTECH SCIENTIFIC SERVICES

RAW DATA FOR THIS STUDY IS KEPT ON FILE AT RALTECH SCIENTIFIC SERVICES, MADISON, WISCONSIN.

RT LAB NUMBER 856940 GUINEA PIG MAXIMIZATION

Test Material: Varisoft 222-90 Lot #SC49-68B 644750

Test Animal: Young adult male guinea pigs were procured, maintained individually in stainless steel cages in temperature and humidity controlled rooms, provided continuous access to Purina Guinea Pig Chow and water and held for an acclimation period of at least 7 days.

Test System: Ten male guinea pigs weighing between 398 and 500 grams were chosen at random and used for this study. The animals were individually housed and identified by animal number and ear tag.

Preparation of Test Material: For the intradermal injections the Freund's Complete Adjuvant Solution was prepared by adding 5 mL of sterile water for injection in 1 mL increments to 5 mL of Freund's Adjuvant.

The 5% solution of test material in sterile water was prepared by taking 0.25 gram of Varisoft 222-90 Lot #SC49-68 644750 and adding sterile water for injection to a total volume of 5.0 mL.

The 5% solution of test material in Freund's Adjuvant was prepared by mixing 0.25 g of Varisoft 222-90 Lot #SC49-68 644750 in 2.5 mL of sterile water and adding 2.5 mL of Freund's Adjuvant in 1.0 mL increments to a total volume of 5.0 mL.

For the topical induction and challenge procedures the Varisoft 222-90 Lot #SC49-68 644750 was applied at 10% w/v and 1.0% w/v suspensions in 0.9% saline, respectively.

Method: A 4.0 x 6.0 cm area was clipped along the midline over the shoulder region. Two rows of three-deep intradermal injections (total of 6 injections) were made within the boundaries of a 2.0 x 4.0 cm area, one row on each side of the midline as follows: 0.05 mL of the prepared Freund's Adjuvant Solution, 0.05 mL of a 5% aqueous test solution, and 0.05 mL of a 5% solution of test material and Freund's Adjuvant Solution.

One week after the injections, the same area was clipped and closely shaved with an electric razor. A 2.0 x 4.0 cm patch of Whatman No. 3 filter paper was saturated with a 10% w/v suspension of Varisoft 222-90 in 0.9% saline, placed over the injection sites, then covered with an overlapping of Blenderm tape and secured by an overwrap of Elastoplast tape. The dressing remained in place for 48 hours.

Two weeks after topical induction the animals received a challenge dose. The hair was removed from a $5.0 \times 5.0 \text{ cm}$ area on the flank by clipping and

shaving as before. A 1.0% w/v suspension of test material in 0.9% saline was applied on a 2.0×2.0 cm piece of filter paper in the same fashion as for topical induction. The patch was sealed to the flank for 24 hours under a 4.0 cm strip of Blenderm tape. Complete occlusion was made by an overwrap with Elastoplast tape wound around the trunk.

Observations: Twenty-four hours following patch removal the test sites were examined for erythema and edema. The sites were examined again at 48 hours after patch removal to detect weak, slowly developing reactions. The test sites were shaved 3 hours prior to the 24 hour reading. The reactions were scored according to the following 4-point scale:

- 0 = no reaction
- l = scattered mild redness
- 2 = moderate and diffuse redness
- 3 = intense redness and swelling

The important statistic in maximization testing is the frequency of sensitization, not the intensity.

Pathology: Any animal that died during the course of the study was subjected to a gross necropsy examination and abnormalities recorded. At study termination all suriving animals were euthanatized and discarded.

RT LAB NUMBER 856940 GUINEA PIG MAXIMIZATION

Test Animal: Albino guinea pigs Source: Dean Daul, Luxemburg, WI Date Animals Received: 4/10/81

Test Material: Varisoft 222-90 Lot #SC49-68 644750

Date Test Started: 4/27/81 Date Test Completed: 5/21/81

| Animal Number | <u>Sex</u> | 24 Hours Right | 48 Hours Right |
|------------------|------------|-------------------|-------------------|
| 64100236 | М | 0 | 0 |
| 64100237 | M | - | - |
| 64100238 | M | 0 | 0 |
| 64100239 | M | 1 | 0 |
| 64100240 | M | Ô | 0 |
| 64100241 | M | Ŏ | 0 |
| 64100242 | M | 3 | 2 |
| 64100243 | M | 1 | 0 |
| 64100244 | M | Ô | 0 |
| 64100245 | M | Ö | 0 |

General Behavior and Appearance:

One animal (No. 64100237) was found dead on 5/9/81. This animal was hypoactive and ataxic on 5/8/81. The only abnormality observed at necropsy was that the stomach was distended with gas and a reddish-brown liquid. This death is not considered treatment related. No signs of sytemic toxicity were observed in any of the remaining nine animals at any observation period during the study.

Normal body weight gains were recorded for four animals during the course of the study. One animal (No. 64100244) exhibited a body weight loss and four animals showed a slight body weight gain during the second week on test. Normal body weight gains were recorded for all animals at the end of the third week on test.

Skin Reactions to Varisoft 222-90 Lot #SC49-68 644750:

Three animals (Nos. 64100239, 64100242, and 64100243) exhibited a sensitization reaction to the test material following the challenge application. Two animals (Nos. 64100239 and 64100243) reacted with a mild redness at 24 hours and one animal (64100242) exhibited an intense redness and swelling at 24 hours and a moderate and diffuse redness at 48 hours. The six remaining animals did not exhibit any reaction to the challenge dose at either the 24 or 48 hour observations.

Conclusion:

Based upon the results obtained, the test material, Varisoft 222-90 Lot #SC49-68 644750, is considered a skin sensitizer in guinea pigs.

Reference:

Magnusson, B. MD, and A. Kligman, PhD, MD, Allergic Contact Dermatitis in the Guinea Pig, Charles C. Thomas, pub., 1970, pp. 113-117.

GUINEA PIG MAXIMIZATION TEST

| Test Compound - | risas+ 222- | .90 | RT No. | (また の ごろ |
|------------------------|-------------|-------------|-------------|-----------------|
| pH Result | NA 50+9 | 02 FAH 030' | Sponsor No. | |
| Date Animals Received | 13/0/14 | | | |
| Date of Intradermal In | | ear Taul | | |
| Date of Topical Applic | | M Sw M | | |
| Date of Challenge | | | | NDD CHI |
| | <u> </u> | <u> </u> | Technician | NDA SE |
| | 24 Hour | rs | 48 Hou | ırs |
| Animal No., Sex | Right | Left | Right | Left |
| 6410- 0236 8 | 0 | | 0 | Lett |
| 0237 07 | 519 81 ER | | NA | |
| 0238 0 | 0 | | 0 | 1 |
| 0239 0 | | | 0 | |
| 0240 07 | 0 | | 0 | - \ |
| 0241 0 | 0 | | 0 | |
| <u> </u> | 3 | | 2 | Y |
| ०२५३ ठी | | , | . 0 | |
| ०२४४ ल | 0 | \ | O | |
| 2245 A | 0 | , | <u> </u> | |
| Technician | Co | | P | |
| Recorded By | SP. | | P | |
| Date 1981 | 5/20 | | JP F/21 | |

NA - NO+ Applicable 5/18/81 NOO

Scoring Code: 0 = Normal, No Reaction

1 = Scattered Mild Redness

2 = Moderate and Diffuse Redness

3 = Intense Redness and Swelling

| REVIEWED | 3¥: | <u> 100</u> | DATE: | 512918 |
|----------|-----|-------------|-------|--------|
|----------|-----|-------------|-------|--------|

O Maximization Dermal Sensitisation In Guinea Pigs - Body Weights

| | Test Group RT No. 856940 | | Test Compound Varisoft 222 |
|----|---------------------------|------------|----------------------------|
| MA | Positive Control Group NA | Vehicle NA | Lot # 50-49-68 6-44750 |

| | | | Animal | Number | | | | T | • |
|-------|---------------|-------|----------------------|--------|-------|-------|-------|-----------------|-----------|
| 6410- | 6410- | 6410- | 6410- | 6410- | 6410- | 6410- | 6410- | 7 | |
| 0236 | 0237 | 0238 | 0239 | 0240 | 0241 | 0242 | 0243 | Tech- nician | Date /98/ |
| 451 | 500 | 449 | 478 | 449 | 398 | 426 | 463 | Jw. | 4/2 |
| 482 | 544 | 517 | 546 | 480 | 436 | 148 | 526 | 1.0 | 5/4 |
| 521 | Pound CRAD | 544 | <i>.</i> 57 <i>7</i> | 483 | 441 | 453 | 584 | MYP | |
| 1012 | 5/9/81 | 633 | 642 | 573 | 540 | 528 | | PID | |
| | | | | | | | | <u> </u> | -2112 |
| | . 🗸 | | | | · | | | | |

| | | Animal Number | | |
|-------|-------|-------------------------|-----------------|------|
| 6410- | 6410- | · | · | T |
| 0244 | 0245 | | Tech- nician | Date |
| 424 | 427 | Scale Used: K-Tron 4809 | | 1981 |
| 41,2 | | Scale Used: | - Sw | 4/27 |
| 446 | 4.3 | K KON 4809 | del | 5/4 |
| | 46.3 | 12-110A 4809 | JAM | 5/11 |
| 531 | 552 | Scale Used: K-Toon 1809 | RUS | 218 |
| | | Scale Used: | | 2118 |
| | | Scale Used: | | |

¹⁾ Form Change Sw 4/27/8/
NA - Not Applicable

Dose Ranze

| Test (| | | Vehicle | | Test | al Vari | 5017 |
|-----------------------------|-------------------|-------------------------------------|----------|----------|-----------|-------------|---------------|
| | | 6 4/3/8 Dul | | Data | Initiato | | <u> 23/81</u> |
| 6410 - Animal No Site | Dose ² | Obser- vation Period (Hrs) | Erythema | Edema | ecimician | Recorded By | 1981 |
| 0191 | 0.5 | NA | NA | | 1100 | | • |
| | | 24 | NA. | NA NA | NDS | 1 SP | 4/23 |
| <u> </u> | 1.070 | 48 | 1 0 | | MR | MR | 4/20 |
| 0191 | 0.5 | NA | NA | NA | PEN | ER | 4/23 |
| (3) | 5.0% | 24 | 0 | 1 0 | 128 | 100 | 4/24 |
| | 10,070 | 48 | 0 | 0 | IUR | ·UR | 4/25 |
| 0/9/ | 0.5 | NA | NA | · NA | M | ER | 4/23 |
| | 10.0% | 24 | 1.0 | 1 0 | 134 | , YE | 4/24 |
| | 1 10.0 10 1 | 48 | 10 | <u> </u> | MR | · me | 4/25 |
| | | na | NA | . NA | | ar . | |
| | | 24 | | ı | | | |
| | | 48 | | • | 1 | i T | • |

XA

a - Dosage applied by technician indicated
 NA - Not Applicable

MA 24 48

Dose Ratice

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

| Test Group: | RT No. <u>85640</u> Venic | =1 Sterile 0.9) Mater Saline La | 121 Varisof 1 2 17 = 50 49-60 |
|-----------------|---------------------------|------------------------------------|----------------------------------|
| Date Animal Rec | eived <u>413/81</u> | - | |
| Source | on Daul sex 9 | Date Initia | ited 4/23/8 |

| | | | 7 | | Tecl | Reco | |
|------------|-------------------|-------------------------------------|---------------------------------------|-------|------------|-------------|-------------|
| Animal No. | Dose ^a | Obser- vation Period (Hrs) | Erythema | Edema | [eclmician | Recorded by | Nate |
| 030 | 0.5 | NA | NA | na | can | ER | 4/23 |
| Θ | 100% | 24 48 | 1.0 | 0 | UR | INR | 4/26 |
| 0130 B | 0.5 | na . | NA. | NA | DEU | ا وي | 4/23 |
| ł | 1.0% | 24 | 0 | 0 | NR | MR | 4/25 |
| 030 | 0.5 | NA | NA | · KA | 1000 | ER | 4/23 |
| (C) | 5.0% | 24 48 | 1.0 1.0 | 0 | NIC | H | 4/25 |
| | | NA | NA | NA. | ř. | 1. | |
| | | 24 | · · · · · · · · · · · · · · · · · · · | | | 1 | |
| | | MA | AK | , HA | | ! | |
| | | 24 | | | | | |

a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION ST

| \Box | Test Gr | oup: [| RT No. <u>25/194</u> | O Venicles | Jenla ().9% Soline | <u>GS</u> Test Materi ∠ <i>∆T</i> | al <i>Vari</i> = SC | S0f+22 49-186 |
|--------|-----------------------------|------------------------|-------------------------------------|--------------|-----------------------|--|------------------------|------------------|
| | Date Ani | Dean (| Day 1 | 8 _ <u> </u> | Date | Initiat | ed | 4/33 |
| | 6410- Asimal No. Site | Dase [®] (m1) | Obser- vation Period (Hrs) | Erythems | Edema | Technician | Recorded By | Date |
| | 0193 D | 0.5 | NA 24 | KA | NA | PCN | ER | 1981 |
| | | 5,0% | 48 | 1.0 | 0 | SY | 1 38 | : 4/24 |
| | 0/93 | 05 | NA |). O | NA NA | NOQ | I LER | 4/26 |
| | B | 10.0% | 24 | /,0 | 1 (.0 | JE | | 4/24 |
| | | | 48 | 1.0 | 1.0 | MR | · W.R | 4/25 |
| | 0193 | 0.5 | NA | NA | · RA | RDS | ER | 4/23 |
| | | 1.0% | 24 | 0 | 0 | 1 | 1 | 4/24 |
| | | 1,070 | . 46 | 0 | | W | UR | 1/25 |
| | | | NA | NA | NA | | # | |
| | 1 | <u> </u> | 2/4 | | | | i l | |
| | | | 48 | | | | i | • |
| | | | NA | NA. | NA. | | | |

a - Dosage applied by technician indicated
 NA - Not Applicable

Head

Dose Ranze

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

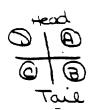
| | | 1100 |
|--------------------|----------------|---|
| Test Group: | RT No. 8510940 | Test Venicle Ster le 0.9% Material Varisot + 222 Saline Lot = SC 49-6864475 |
| Date Animal Receiv | ed v//>/01 | • |

Date Initiated 4/21/81

| | | • | | | Tec | Re | |
|------------------------------|-------------------|-------------------------------------|----------|-------|------------|-------------|--------|
| 6410 - animal No. 517e | Dose ² | Obser- vation Period (Hrs) | Erythema | Edema | [echnician | Recorded by | 1981 |
| 0210 00/20 A | 0.5 | NA | NA | NA | NOW | ER | |
| <u>(A)</u> | 25% | 24 48 | 2.0 | 7.0 | CO | NY | :4/72 |
| 00/20 B | 0.5 | МА | NA | NA | NON | | 4/23 |
| <u>(3)</u> | 50% | 24 | 3.0 | 3.0 | Co | · SR | 14/22 |
| 0 0 2 / 20 | 0.5 | MA | NA | · NA | NDX | | 4/23 |
| | 75% } | 24 48 | 3.0 | 3.0 | Co | FR | |
| 00210 | 0.5 | NA | NA | NA. | XX | - ER | 4/21 |
| | 100% | 24 48 | 3.0 | 3.0 | | N/O | 4/22 |
| | | NA. | AK | NA | | | -/ 5 5 |
| | | 24 | | | | | |

a - Dosage applied by technician indicated NA - Not Applicable

O CORRECTION OF ERER @ Recording error & 4hster



Dose Range

| | | t No. 856940 d 4/3/81 | | • | Materi LOT | | |
|------------------------------|------------------------|-------------------------------------|-------------------------|------------------|---------------|-------------|------|
| 6410 - Animal No. Site | Dose ^a (mi) | Obser- vation Period (Hrs) | Erythema | Edema . | Technician | Recorded By | Date |
| 0167 | 0.5 | NA 24 48 | NA 2.0 | NA 2.0 | NO | ER | 4/21 |
| 0167 | 0.5 25% | NA 24 48 | 3.0 NA 2.0 3.0 | 3.0 NA 1.0 | NON | 100 | 4/21 |
| 0167 | 0.5 50% | NA 24 48 | NA 2.0 3.0 | 2. 0 | NDN | ER 109 | 4/21 |
| 0167 | C. 5 | NA 24 | NA 2.0 | NA 2.0 | 1/50 | ER | 4/21 |

a - Dosage applied by technician indicated
 NA - Not Applicable

48

Tail Head

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

| Test Group: | RT No. 856940 Venicle Ster. 6 0.9% Material Soline Lot # S | Va <u>risoft 222</u> -9 C+9-6864475 |
|-------------|--|--|
| | • | |
| _ | | |

| Date A | nimal | Received | 4/3/ | 81_ | | | | |
|--------|-------|----------|------|-----|---|------|-----------|--------|
| Source | | Denn | Doul | Sex | 3 | Date | Initiated | 4/21/8 |

| | , | | T | | Tech | Rec | |
|---------------------|--|-------------------------------------|------------|-------|------------|-------------|-------------|
| 6410- Animal No. | Dose ² (mi) | Obser- vation Period (Hrs) | Erythema | Edema | Technician | Recorded By | Date |
| 0145 | 0.5 | NA | NA | NA | ACN | SR | 4/21 |
| 8 | 75% | 24 48 | 3.0 | 3.0 | CO | | 4/22 |
| 0145 | 0.5 | na | NA | NA | DON | ER | 4/21 |
| ₿ | 100% | 24 | 2.0 3.0 | 2.0 | CU | 1138 | 4/22 |
| 0145 | 0.5 | NA | Na | · NA | NDX | FR | -4/21 |
| © | 25% - | 24 | 3. O | 2.0 | CO | in | |
| 0/45 | 0.5 | NA | NA | NA | NOR | : 5.8 | 4/21 |
| | 50% | 24 ; 48 j | 2.0 3.0 | 3.0 | CO | 1000 | 4/23 |
| | | #A | NA. | NA | | | , |
| ļ | | 24 | | | | į į | |

ORecording Error 4/2/18/1000

a - Dosage applied by technician indicated

NA - Not Applicable

Dose Ranza

| | DERMAL | SENSITIZATIO | N STUDY IN GUINEA PI | <u>GS</u> |
|-----------------|--------|--------------|--------------------------------|---|
| Test Group: | RT No | ·856940 | Vehicle Sterile 0.9% Soline | Test Material Varisoff 222.9 LOT = SC49.68644750 |
| Date Animal Rec | eived | 412181 | • | |

Date Initiated

| | | | · | | Tecl | Rec | L |
|--------------------|-------------------|-------------------------------------|------------|-------|--------------------|-------------|------|
| 6510- Limil No. | Dose ² | Obser- vation Period (Hrs) | Erythema | Edema | <u> Technician</u> | Recorded By | 1981 |
| 0169 | 0.5 | KA | na | NA | NOR | جع ا | 4/21 |
| <u>(A)</u> | 50% | 24 | 2.0 3.0 | 3.0 | Con | 1100 | 4/22 |
| 0169 | 0.5 | na | NA | NA | NON | ER. | 4/21 |
| <u> </u> | 7570 - | 24 | 2.0 30 | 30 | Ca | MA | 4/22 |
| 0169 | 0.5 | na | NA | · NA | NOO | ER. | 4/21 |
| <u>@</u> | 10070 | 24 48 | 7.0 30 | 13.0 | co | 120 | 4/22 |
| 0169 | 0.5 | KA | na | NA | NDO | ER | 4/21 |
| 0 | 25% | 24 | 2.0 2.0 | : 2.0 | 30 | 120 | 4/32 |
| | | NA. | MA | NA | | | |
| | | 24 | | | | | |

a - Dosage applied by technician indicated NA - Not Applicable

Dose Ranze DERMAL SENSITIZATION STUDY IN GUINEA PIGS

| | | 2. COLVER FIGS |
|-------------|----------------|---|
| Test Group: | PT No CELONO | Test |
| 1000 01000 | M. No. 85/6040 | Venicle Sterilo 0.9% Material Varisoft 222. |
| | | Saline LOT #50 49.6864475 |
| | | • |

Date Animal Received 4/3/81 Date Initiated 4/23/8/ Source Dear's Daul Sex 7

| | | | | | Tec | Rec | |
|---------------|---------------------------|-------------------------------------|----------|----------|-----------|-------------|-------------|
| do inel No. | Dose ² (mi) | Obser- vation Period (Hrs) | Erythems | Edema | ecimician | Recorded by | Date |
| 0191 | 0.5 | na | MA | NA | Ray | - | ! |
| \mathcal{E} | 1.070 | 24 48 | 0 | 3 | NR | 1 JY | 1/24 |
| 0191 | 0.5 | NA | NA | NA. | SEN | ER | 4/25 |
| (3) | 5.0% | 24 48 | 0 | 0 | UR | 156 | 4/24 |
| 0/91 | 0.5 | NA | NA | · NA | 1009 | : UR | 4/25 |
| © | 10.0%; | 24 48 | 1.0 | <u>ပ</u> | MR | NR | 4/24 |
| | | NA | NA | NA | **., | ٠. | |
| | | 24 | · . | | | · | |
| | | NA | MA | NA. | | ! | |
| | | 24 | | | | | |

a - Dosage applied by technician indicated
 NA - Not Applicable

Dose Razze

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

| Test Group: | RT No. <u>854</u> | 940 Vehicl | Sterile 0.9% | Material or | 50/1 22 |
|------------------|-------------------|------------|--------------|-------------|---------|
| | | | Saline | LDT ASC | 19-68 |
| Date Animal Reco | | 7) | _ | | |
| Source | n Daul | _ Sex | Date In | pitiated 4 | 1/23/21 |

| Animal No. | Dose ² | Obser- vation Period (Hrs) | Erythema | Edena | Technician | Recorded By | |
|------------|-------------------|-------------------------------------|------------|---------|------------|-------------|----------------------|
| 0130 | 100% | NA 24 48 | NA /·O | NA © | rog | SR. | 1981 4/23 4/24 |
| 0130 B | 0.5 | NA 24 | NA C | NA C | NOS | ER ST | 4/22 |
| 0130 | 0.5 | NA 24 | NA J. O | · NA | 1003 | ER | 4/25 |
| | 0.0 /0 | 48 NA 24 | /. O | O NA | HZ. | ا | 4/25 |
| | | 48 NA | NA. | HA | | | · |
| | | 24 | | | | | |

a - Dosage applied by technician indicated
 NA - Not Applicable

Dose Range

| Test Gr | oup: | | Venicles | | | alV <i>ari</i> = SC | <u>50++ 2</u> -19-686 |
|-----------------|-------------------|-------------------------------------|----------|--------|---------|------------------------|--------------------------|
| Date Ani | mal Receive | id 4/3/ | 8 | | | | • |
| Source | Dean | Daul | Sex | Date | Ioitiet | ed _ | 4/33 |
| | | | | | = | <u> </u> | |
| 6410- | | · | | ŀ | echa | (eco | Date |
| Animal No. | Dose ² | Obser- vation Period (Hrs) | Erythems | Ed ema | nician | Recorded by | [98] |
| 0193 | 0.5 | NA | NA | NA | PCIA | 50 | : |
| | 5,0% | 24 | 1.0 | 0 | 100 | 138 | 1/23 |
| | 5,070 | 48 | 1.0 | 0 | rik | MR | 4/26 |
| 0193 | 0.5 | MA | NA | NA | PCN | ER | 4/23 |
| $ \mathscr{B} $ | 10.0% | 24 | 1,0 | 1.0 | J.P | 1 | 4/24 |
| | 100/01 | 48 | 1.0 | 1.0 | MR | We | 1/25 |
| 0193 | 0.5 | NA | NA | . KA | 100 | ER | 4/23 |
| | 1.0% | 24 | ٥ | 0 | 13 | R | 4/24 |
| | 1.070 | 48 | 0 | | WR | UR | 1/25 |
| | | NA | NA | NA | | ÷ . | |
| | ! | 2/ | i | | | | |
| | | 48 | | | | i I | • |
| | | NA | NA | 164 | | | |
| | L | 24 | | | | - | |
| 1 | | 48 | | | | | |

a - Dosage applied by technician indicated
 NA - Not Applicable

Head

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

| Test Group: | RT No. 8516940 | Test Venicle Sten le 0.9% Material Varisoft 222 Saline Lot = \$2.49-686447 | | | |
|--------------------|----------------|--|--|--|--|
| Date Animal Receiv | red 4//2/01 | • | | | |

Date Initiated 4/21/81

| | | | | | Tech | Rec | |
|------------------------------|-------------------|-------------------------------------|----------|-------------------------|--------|-------------|------|
| 6410 - Animal No. Site | Dose ^a | Obser- vation Period (Hrs) | Erythema | Edema | mician | Recorded By | 1981 |
| 0210 00/20 | 0.5 | NA. | NA | NA | NDR | ١٤٤ | 4/21 |
| (A) | 25% | 24 48 | 2.0 | /· () | CO | | 4/23 |
| 9770 B | 0.5 | NA | NA | NA | NON | SR | 4/21 |
| (3) | 50% | 24 48 | 3.0 | 3.0 | Co | NIX | 4/22 |
| 00120 | 0.5 | NA | NA NA | · NA | NON | SQ. | 4/23 |
| ۵ | 75% } | 24 48 | 3.0 | 3.0 | Co | NOW | 4/22 |
| 8210 | 0.5 | Na | NA | NA | NOW | ER | 4/21 |
| | 100% | 24 48 | 1 3.0 | · 2. <u>()</u> · 3.0 | 37 | 1 | 4/12 |
| | | - NA | NA | NA | | | |
| | - | 24 48 | | | | ! | |

a - Dosage applied by technician indicated NA - Not Applicable

O COLLECTION OFFERER @ Recording error & 4/2ster



Dose Range

| Source | | | | | | | |
|---------------------------|------------------------|-------------------------------------|------------------|---------------|-----------|---------------|--------|
| | <u> Pean l</u> | Saul : | Sex <u>3</u> | Date : | loitiet | ed _ <u> </u> | 4211 |
| 0410 - 010 - No. 5:1e | Dose ² (mi) | Obser- vation Period (Hrs) | Erythems | Ed ema | ecimician | Recorded by | 1981 |
| 0167 | 0.5 | NA | NA | NA | NDW | ER | 4/21 |
| © | 100% | 24 | 2.0 | 2.0 | Co | وديا | 4/22 |
| 0167 | 0.5 | NA | NA | NA NA | NO | ا ۾ءِ ا | 4/21 |
| 6 | 25% | 24 | 2.0 | 1.0 | Co | PC1 | 4/22 |
| | 1 | | 7.0 | 1 30 | 1 | ; | _ |
| 0167 | 0.5 | NA | N/A | N.A. | | 1 60 1 | ·41- · |
| 0167 © | 0.5 | NA 24 48 | NA 2,0 3.0 | 2. 0 3. 0 | 100 | | 4/21 |

a - Dosage applied by technician indicated
 NA - Not Applicable

24 48

Tail -

Dose Ranze

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Test Group: RT No. <u>856940</u> Vehicle <u>Ster. le 0.97</u> Material <u>Var. 504 + 222</u>-90

Soline LCT # SC 49-68644750

Date Animal Received 4/3/8/
Source Dehn Doul Sex 7 Date Initiated 4/21/8/

| | | | | | Tech | Rec | |
|---------------------|---------------------------|-------------------------------------|-------------|-------|----------|-------------|-------|
| 6410- Animal No. | Dose ² (mi) | Obser- vation Period (Hrs) | Erythema | Edena | nician | Recorded by | 1981 |
| 0145 | 0.5 | NA | KA | NA | W | 68 | 4/21 |
| | 75% | 24 48 | 3.0 | 3.0 | CO | NOO! | 4/22 |
| 0145 | 0.5 | na | NA | NA | 201 | ER | 4/21 |
| ® | 100% | 24 | 2.0 3.0 | 3.0 | CU | UD9 | |
| 0145 | 0.5 | NA | Na | · NA | NDO | ER. | -4/21 |
| @ | 25% - | 24 48 | 2. O 3.0 | 2.0 | CO | TO | 4/22 |
| 0145 | 0.5 | NA | NA | NA | NOW | E.R. | 4/21 |
| (D) | 50% | 24 48 | 2.0 3.0 | 3.0 | CO | 130 | 4/23 |
| | | #A 24 | XA | NA | <u> </u> | | |
| | | 48 | | | | | |

Orecording Error 4/21/81 WX

a - Dosage applied by technician indicated

NA - Not Applicable

| | DEMINE SENSITIONI | ON STODY IN GUINEA P | 163 |
|-----------------|-------------------|----------------------|----------------------------------|
| Test Group: | RT No. 856940 | Venicle Sterile 0.9% | Test Material Varisoft 222.90 |
| ŕ | • | Soline | |
| Date Animal Rec | eived 4.2/81 | • | |
| Source Do | an Daul ser | E _ d Dete | Initiated |

| | | | | | [ec] | Rec | |
|-----------------------------|------------------------|-------------------------------------|------------|----------------|-------------------|-------------|-------------|
| 6510- Animal No. Site | Dose ² (mi) | Obser- vation Period (Hrs) | Erythema | Edema | <u>recimician</u> | Recorded By | Date |
| 0169 | 0.5 | na | NA | NA | NON | FR | 4/21 |
| <u>(A)</u> | 50% | 24 | 7.0 3.0 | 3.0 | CS | 1133 | 4/22 |
| 0169 | 0.5 | NA | NA | NA | NDX | FR | 14/21 |
| <u> </u> | 75701 | 24 · 48 | 2.0 | 3.0 | Co | NO | 4/22 |
| 0169 | 0.5 | ЖA | MA | · NA | 1200 | ! ER | -4/21 |
| <u>Q</u> | 100701 | 24 48 | 3.0 | 13.0 | 100 | 120 | 4/22 |
| 0169 | 0.5 | NA | NA | NA | NDA | ER | 4/21 |
| 0 | 25% | 24 48 | 2.0 | : 1.0 : 2.0 | 100 | 133 | 4/22 |
| | | #4 | NA | NA | | ! | |
| | | 24 48 | | | | ! | |

a - Dosage applied by technician indicated
 NA - Not Applicable

GUINEA PIG MAXIMIZATION STUDY OF VARISOFT 222-90 LOT 1183-K 184-857

SPONSOR:

SHEREX CHEMICAL CO.

DUBLIN, OHIO

STUDY NO.

877521

INITIATION: COMPLETION:

8/6/81 8/30/81

REPORTED:

9/15/81

SAMPLE: VARISOFT 222-90 LOT 1183-K 184-857

ENCLOSED: METHOD, PAGES 2 AND 3

SUMMARY, PAGE 4 RAW DATA APPENDIX

SIGNED:

NANCY J. ALBRECHT, BA

TECHNICAL SUPERVISOR

GARY W. THOMPSON, BS

MANAGER, ACUTE TOXICOLOGY

STUDY DIRECTOR

BY AND FOR RALTECH SCIENTIFIC SERVICES

RAW DATA FOR THIS STUDY IS KEPT ON FILE AT RALTECH SCIENTIFIC SERVICES, MADISON, WISCONSIN.

RT LAB NUMBER 877521
GUINEA PIG MAXIMIZATION

Test Material: Varisoft 222-90 Lot 1183-K 184-857

Test Animal: Young adult male guinea pigs were procured, maintained individually in galvanized steel cages in temperature and humidity controlled rooms, provided continuous access to Purina Guinea Pig Chow and water and held for an acclimation period of at least 7 days.

Test System: Ten male guinea pigs weighing between 356 and 430 grams were chosen at random and used for this study. The animals were individually housed and identified by animal number and ear tag.

Preparation of Test Material: For the intradermal injections the Freund's Complete Adjuvant Solution was prepared by adding 5.0 ml of sterile water for injection (in 1.0 ml increments) to 5.0 ml of Freund's Adjuvant.

The 5% solution of test material in sterile water was prepared by taking 0.25 gram of Varisoft 222-90 Lot 1183-K 184-857 and adding sterile water for injection to a total volume of 5.0 ml.

The 5% solution of test material in Freund's Adjuvant was prepared by dissolving 0.25 gram of Varisoft 222-90 Lot 1183-K 184-857 in 2.5 ml of sterile water and adding 2.5 ml of Freund's Adjuvant (in 1.0 ml increments) to a total volume of 5.0 ml

For the topical induction the Varisoft 222-90 Lot 1183-K 184-857 was dosed at a 20% w/v mixture in sterile 0.9% saline. For the challenge application the Varisoft 222-90 was dosed at a 0.1% w/v mixture in sterile 0.9% saline.

Method: A 4.0 x 6.0 cm area was clipped along the midline over the shoulder region. Two rows of three-deep intradermal injections (total of 6 injections) were made within the boundaries of a 2.0 x 4.0 cm area, one row on each side of the midline as follows: 0.05 ml of the prepared Freund's Adjuvant Solution, 0.05 ml of the 5% aqueous test solution, and 0.05 ml of the 5% solution of test material in Freund's Adjuvant.

One week after the injections, the same area was clipped and closely shaved with an electric razor. A 2.0 x 4.0 cm patch of Whatman No. 3 filter paper was saturated with a 20% w/v mixture of Varisoft 222-90 in sterile 0.9% saline, placed over the injection sites, then covered with an overlapping of Blenderm tape and secured by an overwrap of Elastoplast tape. The dressing remained in place for 48 hours.

Two weeks after topical induction the animals received a challenge dose. The hair was removed from a 5.0 x 5.0 cm area on the flank by clipping and

RT LAB NUMBER 877521
GUINEA PIG MAXIMIZATION

shaving as before. A 0.1% w/v suspension of test material in 0.9% saline was applied on a 2.0×2.0 cm piece of filter paper in the same fashion as for topical induction. The patch was sealed to the flank for 24 hours under a 4.0 cm strip of Blenderm tape. Complete occlusion was made by an overwrap with Elastoplast tape wound around the trunk.

Observations: Twenty-four hours following patch removal the test sites were examined for erythema and edema. The sites were examined again at 48 hours after patch removal to detect weak, slowly developing reactions. The test sites were shaved 3 hours prior to the 24 hour reading. The reactions were scored according to the following 4-point scale:

- 0 = no reaction
- 1 = scattered mild redness
- 2 = moderate and diffuse redness
- 3 = intense redness and-swelling

The important statistic in maximization testing is the frequency of sensitization, not the intensity.

RT LAB NUMBER 877521
GUINEA PIG MAXIMIZATION

Test Animal: Albino guinea pigs Source: Dean Daul, Luxemburg, WI Date Animals Received: 7/29/81

Test Material: Varisoft 222-90 Lot 1183-K 184-857

Date Test Started: 8/6/81 Date Test Completed: 8/30/81

| Animal Number | Sex | 24 Hours Right | 48 Hours Right |
|------------------|-----|-------------------|-------------------|
| 64100448 | м | 0 | 0 |
| 64100449 | M | 0 | 0 |
| 64100450 | M | 0 | 0 |
| 64100451 | М | 0 | 0 |
| 64100452 | M | 0 | 0 |
| 64100453 | M | 0 | 0 |
| 64100454 | M | 0 | 0 |
| 64100455 | M | 0 | 1.0 |
| 64100456 | M | Ō | 0 |
| 64100457 | M | 0 | 0 |

General Behavior and Appearance:

All of the guinea pigs used in this study appeared normal throughout the study period. Normal body weight gains were recorded for all animals during the course of the study, with the exception of one animal (No. 64100450) that exhibited a slight weight loss during the second week on test.

Skin Reactions to Varisoft 222-90: Lot 1183-K 184-857

One animal (No. 64100455) reacted to the challenge dose with a mild redness at the 48 hour observation. Nine animals did not exhibit any reaction to the challenge application at either the 24 or 48 hour observations.

Conclusions:

This test material is not considered a strong skin sensitizer in guinea pigs.

Reference:

Magnusson, B. MD, and A. Kligman, PhD, MD, Allergic Contact Dermatitis in the Guinea Pig, Charles C. Thomas, pub., 1970, pp. 113-117.

GUINEA PIG MAXIMIZATION TEST

| Test Compound Varisoft | 222-90:Lat 118 | 3-K 184-85 | 7 RT No. 87 | 1521 |
|------------------------|----------------|------------|-------------|----------|
| pH Result | Α | | Sponsor No. | NA |
| Date Animals Received | 7/29/81 | | Source Do | anDaul |
| Date of Intradermal In | jections 💮 | 10181 | Technician | M |
| Date of Topical Applic | ation 8 | 3/81 | Technician | ER |
| Date of Challenge | 8/27/81 | | Technician | ER. |
| | 24 Hours | | 48 Hou | :s |
| Animal No., Sex | Right | Left | Right | Left |
| <u>0448</u> | 0 | | 0 | \ |
| 0449 8 | 0 | | 0 | |
| 0450 3 | 0 | | 0 | |
| 0451 8 | 0 | | 0 | |
| 0452 8 | 0 | | 0 | |
| 0453 8 | · O | | 0 | |
| 0454 8 | 0 | | 0 | |
| 0455 3 | 0 | | 1.0 | |
| 0456 3 | 0 | · | 0 | |
| 0457 8 | 0 | | 0 | |
| Technician | ER | | gyp | |
| Recorded By | M | | ER. | |
| Date 1981 | 8/29 | T | 8/30 | |

Scoring Code: 0 = Normal, No Reaction 1 = Scattered Mild Redness

2 = Moderate and Diffuse Redness
3 = Intense Redness and Swelling

| REVIEWED | BY: | DATE: | 9 | 14 | 1 |
|----------|-----|-------|---|----|---|
| | | | | | |

Dermal Sensitization In Guines Pigs - Body Weights

Varisoft 222-90

Test Group RT No. 87752| Vehicle NA Test Compound Lot 1183-K 184-8

NA Positive Control Group NA Vehicle NA

| | | | Animal | Number | | | | | |
|------|---------------|---------------|--------|---------------|---------------|---------------|---------------|-----------------|--------------|
| 0448 | 0449 6410- | 6410- 0450 | 0451 | 6410- 0452 | 6410- 0453 | 6410- 0454 | 6410- 0455 | Tech- nicien | Date 1981 |
| 411 | 389 | 407 | 427 | 421 | 388 | 401 | 430 | ER. | 8/6 |
| 460 | 449 | 461 | 506 | 485 | 432 | 444 | 485 | ER | 8/13 |
| 479 | 467 | 458 | 526 | 503 | 452 | 456 | 500 | des | 8/20 |
| 584 | 556 | 545 | 564 | 552 | 515 | 534 | 59b | 76 | |
| | | | | | , | | | | |
| | | | | | | | | | |

| | | Animal Number | 7 | |
|------------------------|---------------|--------------------------|-----------------|--------------|
| 6410 - 04 56 | 6410- 0457 | | Tech- nician | Date 1981 |
| 413 | 356 | Scale Used: K.Tron 4809 | ٤٩ | 8/6 |
| 462 | 410 | Scale Used: K. Tron 4809 | ۽ جي | 8/13 |
| 478 | 440 | Scale Used: K. IRON 4809 | de | 8/20 |
| 559 | 501 | Scale Used: K-Tron 4809 | SP | 8/27 |
| | | Scale Used: | | |
| | _ | _ Scale Used: | | |

Dermal Sensitization in Guines Pigs - Daily Observations Varisoft 222-90:

Test Group RT No. 87752 | Vehicle NA Test Compound Lot 1183-K 184-857

NA Positive Control Group NA Vehicle NA Room No. 3

| | | An | imal Numb | er | | • | |] | |
|--------|---------------|---------------|---------------|---------------|-------|-------|---------------|--------|---------------|
| 6410- | 6410- | 6410- | 6410- | 6410- | 6410- | 6410- | 6410 | Tech- | |
| 0448 | 0449 | OH50 | 0451 | 0452 | 0453 | 0454 | 0455 | nicien | 1981 |
| N | N | . N | Ν | \mathcal{N} | N | N | N | NIN | 8/20 |
| N | N | Ν | N | Ν | N | Ν | N | ER. | 8/7 |
| N | N | N | Ν | Ν | Ν | N | ·N | εQ | 8/8 |
| N | N | N | N | N | N | N | N | Me | 819 |
| N | N | \mathcal{N} | \mathcal{N} | \mathcal{N} | 2 | 2 | \mathcal{X} | des | 8110 |
| N | N | Ν | N | N | N | V | ν | | 8/11 |
| N | a | N | N | N | N | N | N | Sh | 8/12 |
| N | Ν | N | Ν | N | N | 2 | 2 | ER | 8/13 |
| N | N | N | Ν | N | N | 7 | N | Æ | 8/14 |
| - 17 | Ň | N | N . | N | N | N | N | عاد | 8/15 |
| N | N | N | N | N | N | N | N. | IR | 8/16 |
| N | N | , la | کر | (بر | Ŋ | N | N | de | 8/17 |
| N | N | N | N | N | N | 1/ | 11 | ir | 8/19 |
| N | N | N | N | N | N | N | N | ER | 8/19 |
| N | N | N | N | N | N | N | N | ER | 8/20 |
| N | N | _ N | N | N | Ŋ | N | N | de | 8/21 |
| N | N | N | N | N | V | V | N | XI | <i>शि</i> य व |
| \sim | \mathcal{N} | N | N | N | N | N. | N | NDO | 8/23 |

N - No Visible Abnormalities

| | Dermal | Sensitiza | ation in G | wines Pi | zs - Dail | y Observa | tions | /arianco | - 422-90 |
|----------|-----------|-----------|---------------|--|-----------|-----------|----------|-----------|-----------------|
| × r | est Group | RT No. 8 | 377521 | Vehicle | NA | Test Co | mbonnq 7 | ot 1183-1 | <u> 184-</u> 85 |
| NA Po | sitive C | ontrol Gr | oup <u>NA</u> | Veh | icle^ | VARo | om No | 3 | |
| | | | | | | | | | |
| | | An | imal Numbe | er . | | • | | | |
| | 6410- | | | | | i I | | Tech- | Date |
| 0456 | 0457 | | | | | | | | 1981 |
| N | N | | | | | 1 | | NX | 8/20 |
| IV | | | | | | | | | 8/7 |
| N | N | | | | | | | ER | 8/8 |
| N | . I | | | | | | | 50 440 | 819 |
| N_ | 3 | | | | | | | Me | 8/10 |
| 7 | | | | \ | | | | | |
| <u>N</u> | N | | | _ | | | | JR | 8/11 |
| _ | <u> </u> | | | \ | | | | Da | 8/12 |
| N | N. | | | | | | | SR. | 8/13 |
| N | N | | | | | | | 52 | 8/14 |
| N | N | | | | | | · · | JK | 8/15 |
| N | N | | | | | | | 1K | 8/16 |
| J | N | | | | | \ | | de | 8/17 |
| N | W | | | | | | | ik | 8/18 |
| N | N | | | | | | | ER | 8/19 |
| N | N | | | | | | | ER. | 8/20 |
| N | N | | | | | | | des | 8/4 |
| N | N | | | | | | 1 | DEN | 7122 |
| 1/ | N | | | | | | \ | NJ | 8/23 |

N - No Visible Abnormalities

| | Dermal Sensitization in Guinea Pigs - Daily Observa | tions Varisoft 222-90 |
|----|---|-------------------------|
| X | Test Group RT No. 87752 Vehicle .NA Test Con | mpoundlet 1183-K 184-85 |
| NA | Positive Control Group NA Vehicle NA Ro | om No. 3 |

| | | An | imal Numb | | | • | | | |
|---------------|---------------|---------------|---------------|----------|---|---------------|---------------------|-----|--------------|
| 6410- 0448 | 6410- 0449 | 6410- 0450 | 6410- 0451 | ì | | 6410- 0454 | <i>6410</i> 0455 | | Date 1981 |
| W | N | N | N | N | N | N | N | dw | 8/24 |
| 1/ | N | N | N | N | N | N | N | K | 8/25 |
| N | N | N | N. | N | N | N | N | ER | 8/26 |
| N | N | N | N | N | N | N | N | JR | 8/27 |
| N | N | N | N | N | N | N | N | JP. | RIZR |
| 2 | 2 | N | 2 | N | 2 | ~ | N | NO | 8/29 |
| N | N | N . | N | N | N | N | N | εR | 8 30 |
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N - No Visible Abnormalities

| | Dermal | Sensitiz | stion in (| Guines Pi | gs - Dail | y Observa | tions | /2=i e ~ C | - 222-90 |
|---------------|------------------------|----------|------------|------------|-----------|-----------|----------|-----------------|-----------------|
| X r | est Group | RT No. | 377521 | Vehicle | NA | _ Test Co | mpound j | -+ 1183-1 | <u> 184-</u> 85 |
| | | | oupNA | | | | | | |
| | | | | | | | | | |
| | | An | inal Numb | 8 2 | | • | | | |
| 6410- 0456 | 6410- 04 5 7 | | | | · | | | Tech- nician | Data 1981 |
| N | N | | | | | | | dal | 8/24 |
| N | N | | | _ | | | | JR | 8/25 |
| N | N | | | | | | | ER | 8/26 |
| N | N | | | | | | |)R | 8/27 |
| N | N | | | | | | | JR | श्रीष्ट |
| 12 | N | | | | | | | 10 | 8/29 |
| N | N | | | | | | | ER | 8 30 |
| | | | | | | | | | |
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N - No Visible Abnormalities

Dose Ratize

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Varisoft 222-90

sterile Test

Test Group: RT No. 87752 | Venicle 0.990 Saling Material Lot 1183-K 184-8

Lot #23-712-DM-02

Date Animal Received _ 7 29 81 Date Initiated 8 20 81 Source Dean Daw

| | | | | | Teclu | Reco | Ę. |
|---------------|------------------------|-------------------------------------|----------|-----------|-------------|--|--------------|
| Acimal No. | Dose ² (ml) | Obser- vacion Period (Ers) | Erythema | Edema | Technician | Recorded By | 1981 |
| 6410- 0478 | 0.1% | NA | NA | NA. | 6. b | ER | 8 20 |
| 0470 | | 24 | 0 | 0 | ୧୧ | de | 8/21 |
| | 0.5 | 48 | | | 13 | RU! | 109 2 |
| 6410 - | 0.1% | NA | NA | NA. | çe | ER | alzo |
| 0478 | 0.5 | 24 | 0 | 1 0 | روع | de | 2/21 |
| | 10.5 | . 48 | | <u> </u> | nid | N.D. | maa |
| | | AK | NA | · NA | | 1 | |
| | | 24 | | 1 | | : | - |
| | | 48 | | <u>_i</u> | ! | : | |
| | | NA | NA | NA | | | |
| 1 | | 24 | | i | | 1 + | <u> </u> |
| | | 48 | | <u> </u> | 1 | ! | |
| , | | MA | AK | NA | | ! | |
| | | 24 | | | <u> </u> | | |
| | | 48 | | | ! | ــــــــــــــــــــــــــــــــــــــ | |

a - Dosage applied by technician indicated

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Varisoft 222-90

Sterile

Test

Tesr Group:

RT No. 877521 Vehicle 0.990 saline Material Lot 1183-K 184-8

| | | | | | = | - |
|---------------|------------------------|-------------------------------------|----------|---------|------------|--------------|
| Animal No. | Dose ^a (ml) | Obser- vation Period (Hrs) | Erythems | Ed ema. | recimician | Recorded By |
| | 1.0% | NA | NA | NA | وي | EQ. |
| 0417 | | 24 | | | 108 | 1 MP |
| | 0.5 | 4.8 | 1 0 | 0 | MP. | j w 2 |
| | 10% | NA | NA. | NA | وو | ER |
| 1140 | 1 | 24 | 0 | 0 | I WK | we |
| | 0.5 | 48 | 0 | ٥ | ! Me. | W2 |
| | 20.% | NA | NA | · NA | ER | : ER |
| 0417 | _ [| 24 | 1.5 | 1 1.0 | MR | W. |
| | 0.5 | 48 | 2.0 | 1.0 | I We- | MR |
| | 50% | NA | NA | NA | وو_ | عع |
| 0417 | 0.5 | 24 | 3.0 | - と・() | · WP | ME |
| 1 () — 1 1 | | | | 25 | | |

a - Dosage applied by technicism indicated

AB

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Varisoft 222-90:

Test Group:

RT No. 87752 Vehicleo.990 saline Material Lot 1183-K 184-857

Date Animal Received 7/10/81

Source Dean Daul Sex 8 Dece Initiated 8/7/81

| | | | | | Tech | Reco | ינו |
|------------|---------------------------|-------------------------------------|----------|--------|------------|-------------|-----------|
| Animal No. | Dose ² (ml) | Obser- vation Period (Hrs) | Erythema | Edema | [ec]miclan | Recorded By |) 1981 |
| 07.01 | 10% | NA | NA | AK | وو | ER | 8/7 |
| 0381 | 0.5 | 24 48 | 1.0 | 0 | WK | MR | 96 8 9 |
| | 20% | NA | NA | NA | ėe | ER | 817 |
| 0381 | 0.5 | 24 | 1.0 | 1.0 | MR | | 86 |
| | 50% | NA | NA | · NA | <u>دو</u> | ۽ جو | 8/7 |
| 0381 | 0.5 | 24 4 8 | 2.5 | 1 3.() | WE | MP. | 818 |
| | 1.0% | NA | NA. | NA | جو | ER. | 8/7 |
| 0381 | 0.5 | 24 48 | 15 | 1.0 | MAR MAR | NAR | 8/8 |
| | | 194 | AK | NA | - | | |
| | | 24 48 | | | | | |

a - Dosage applied by technician indicated

Head

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Varisoft 222-90

sterile

Test Group:

RT No. 877521 Vehicleo.990 Saling Material Lot 1183K 184-85

Source Dean Dau

| | | | _ | ī. | (ech | Reco | Da . |
|------------|------------------------|-------------------------------------|------------|-------|------------|-------------|------|
| Animal No. | Dose ² (ml) | Obser- vacion Period (Ars) | Erythema | Edema | Technician | Recorded by | 1981 |
| | 20% | na_ | NA | NA | e R | ER | ยา |
| 386 | 0.5 | 24 48 | 1.0 | 1.0 | MR. | I ME | 8 |
| 701 | 50% | MA | Ä | NA | ٤٤ | | 8/7 |
| 386 | 0.5 | 24 48 | 3.0 2.5 | 2.5 | INC. | NVE | GIII |
| | 1.0% | NA | NA | · NA | ER | جو. | 817 |
| 386 | 0.5 | 24 48 | 0 | + 8 | MR | NR | 98 |
| 701 | 10% | NA | NA | NA | ερ | ER | 8/7 |
| 386 | 0.5 | 24 48 | 1.0 | 00 | Me | INP | 89 |
| | | NA - | NA. | NA. | ļ | | 1 |
| | | 24 48 | | | | | |

a - Dosage applied by technician indicated

:up:

Dose Ranze

DERMAL SENSITIZATION STUDY IN GUINEA PIGS
Sterile Te

Varisoft 222-90:

Test

RT No. 87752 | Venicle 0.990 saline Material Lot 1183K 184-857

7/10/81 sal Received Date Initiated 8/7/8/ Obser-Edema Dose Erythems vacion (m1) Period 1981 (Hrs) 50% NA 1.0% NA 24 0.5 10% WE 0.5 W/Z 20% NA MA 24 48 NA 24

e applied by technician indicated pplicable

GUINEA PIG MAXIMIZATION STUDY OF VARISOFT 222-90 LOT 1184-K 184-857

SPONSOR:

SHEREX CHEMICAL CO.

DUBLIN, OHIO

STUDY NO.

877522

INITIATION: 8/6/81

COMPLETION: 8/30/81 REPORTED:

9/15/81

SAMPLE: VARISOFT 222-90 LOT 1184K 184-857

ENCLOSED: METHOD, PAGES 2 AND 3

SUMMARY, PAGE 4 RAW DATA APPENDIX

SIGNED:

TECHNICAL SUPERVISOR

GARY W. THOM SON, BS

MANAGER, ACUTE TOXICOLOGY

STUDY DIRECTOR

BY AND FOR RALTECH SCIENTIFIC SERVICES

RAW DATA FOR THIS STUDY IS KEPT ON FILE AT RALTECH SCIENTIFIC SERVICES, MADISON, WISCONSIN.

Test Material: Varisoft 222-90 Lot 1184-K 184-857

Test Animal: Young adult male guinea pigs were procured, maintained individually in galvanized steel cages in temperature and humidity controlled rooms, provided continuous access to Purina Guinea Pig Chow and water and held for an acclimation period of at least 7 days.

Test System: Ten male guinea pigs weighing between 368 and 428 grams were chosen at random, and used for this study. The animals were individually housed and identified by animal number and ear tag.

Preparation of Test Material: For the intradermal injections the Freund's Complete Adjuvant Solution was prepared by adding 5.0 ml of sterile water for injection (in 1.0 ml increments) to 5.0 ml of Freund's Adjuvant.

The 5% solution of test material in sterile water was prepared by taking 0.25 gram of Varisoft 222-90 Lot 1184-K 184-857 and adding sterile water for injection to a total volume of 5.0 ml.

The 5% solution of test material in Freund's Adjuvant was prepared by dissolving 0.25 gram of Varisoft 222-90 Lot 1184-K 184-857 in 2.5 ml of sterile water and adding 2.5 ml of Freund's Adjuvant (in 1.0 ml increments) to a total volume of 5.0 ml

For the topical induction the Varisoft 222-90 Lot 1184-K 184-857 was dosed at a 20% w/v mixture in sterile 0.9% saline. For the challenge application the Varisoft 222-90 was dosed at a 0.1% w/v mixture in sterile 0.9% saline.

Method: A 4.0 x 6.0 cm area was clipped along the midline over the shoulder region. Two rows of three-deep intradermal injections (total of 6 injections) were made within the boundaries of a 2.0 x 4.0 cm area, one row on each side of the midline as follows: 0.05 ml of the prepared Freund's Adjuvant Solution, 0.05 ml of the 5% aqueous test solution, and 0.05 ml of the 5% solution of test material in Freund's Adjuvant.

One week after the injections, the same area was clipped and closely shaved with an electric razor. A 2.0 x 4.0 cm patch of Whatman No. 3 filter paper was saturated with a 20% w/v suspension of Varisoft 222-90 in sterile 0.9% saline, placed over the injection sites, then covered with an overlapping of Blenderm tape and secured by an overwrap of Elastoplast tape. The dressing remained in place for 48 hours.

Two weeks after topical induction the animals received a challenge dose. The hair was removed from a 5.0 x 5.0 cm area on the flank by clipping and

shaving as before. A 0.1% w/v suspension of test material in 0.9% saline was applied on a 2.0 x 2.0 cm piece of filter paper in the same fashion as for topical induction. The patch was sealed to the flank for 24 hours under a 4.0 cm strip of Blenderm tape. Complete occlusion was made by an overwrap with Elastoplast tape wound around the trunk.

Observations: Twenty-four hours following patch removal the test sites were examined for erythema and edema. The sites were examined again at 48 hours after patch removal to detect weak, slowly developing reactions. The test sites were shaved 3 hours prior to the 24 hour reading. The reactions were scored according to the following 4-point scale:

- 0 = no reaction
- l = scattered mild redness
- 2 = moderate and diffuse redness
- 3 = intense redness and swelling

The important statistic in maximization testing is the frequency of sensitization, not the intensity.

Test Animal: Albino guinea pigs Source: Dean Daul, Luxemburg, WI Date Animals Received: 7/29/81

Test Material: Varisoft 222-90 Lot 1184-K 184-857

Date Test Started: 8/6/81 Date Test Completed: 8/30/81

| Animal Number | 8 | 24 Hours | 48 Hours |
|------------------|-----|----------|----------|
| Number | Sex | Right | Right |
| 64100463 | М | 0 | 0 |
| 64100464 | M | 0 | 0 |
| 64100465 | M | 0 | 0 |
| 64100466 | M | 0 | 0 |
| 64100467 | М | 0 | 0 |
| 64100468 | M | 1.0 | 1.0 |
| 64100469 | M | 0 | 0 |
| 64100470 | M | 0 | 0 |
| 64100471 | M | 0 | 0 |
| 64100473 | M | 0 | 0 |

General Behavior and Appearance:

One animal (No. 64100463) exhibited diarrhea on study Days 9, 11, 12, and 13 and was observed with a red anal discharge on study Day 10. This animal was hypoactive and ataxic from Day 9 through Day 13 of the study. Another animal (No. 64100465) exhibited diarrhea on Day 23 of the study. Both of these animals appeared normal at all other observation periods. The remaining eight guinea pigs used in this study appeared normal throughout the study period.

With the exception of two animals (Nos. 64100463 and 64100466) that exhibited a loss in body weight and one animal (No. 64100465) that had a slight body weight gain at the end of the second week on test, normal body weight gains were recorded for all animals during the course of the study.

Skin Reactions to Varisoft 222-90: Lot 1184-K 184-857:

One animal (No. 64100468) reacted to the challenge dose with a mild redness at the 24 and 48 hour observations. Nine animals did not exhibit any reaction to the challenge application at either the 24 or 48 hour observations.

Conclusions:

This test material is not considered a strong skin sensitizer in guinea pigs.

Reference:

Mangusson, B. MD, and A. Kligman, PhD, MD. Allergic Contact Dermatitis in the Guinea Pig, Charles C. Thomas, pub., 1970, pp. 113-117.

GUINEA PIG MAXIMIZATION TEST

| Test Compound \ | /arisof | - 222 -90 : Lat | 1184-K 184-8 | 57RT No87 | 1522 | | | | |
|-----------------|----------|--|--------------|------------------|---------------------------------------|--|--|--|--|
| pH Result | | | | Sponsor No. | | | | | |
| Date Animals Re | eceived | 7/29/81 | | Source Dean Daul | | | | | |
| Date of Intrade | ermal In | jections $\longrightarrow \mathcal{P}$ | 15/81 | Technician | | | | | |
| Date of Topical | L Applic | ation 8 | 13 81 | Technician | EP. | | | | |
| | | 8/27 | • | Technician | | | | | |
| | | · | | | · · · · · · · · · · · · · · · · · · · | | | | |
| | | 24 Hou | rs | 48 Hou | rs | | | | |
| Animal No., Sea | \$ | Right | Left | Right | Left | | | | |
| 6410-0463 | 3 | 0 | 1 | 0 | | | | | |
| 0464 | 8 | 0 | | 0 | | | | | |
| 0465 | 8 | 0 | | 0 | | | | | |
| | 8 | 0 | | 0 | | | | | |
| 0467 | 8 | O ['] | | 0 | | | | | |
| 0468 | 8 | 1.0 | | 1.0 | | | | | |
| 0469 | 3 | <u> </u> | | 0 | | | | | |
| O 1 10 | 8 | 0 | . \ | 0 | | | | | |
| 1740 | 8 | 0 | | 0 + | | | | | |
| 0473 | 8 | 0 | | 0 | | | | | |
| Technician | | ££, | | gry | | | | | |
| Recorded By | | TP | | 5 6 | | | | | |
| Date -19 | 81 | 8/29 | | 8/30 | | | | | |

Scoring Code: 0 = Normal, No Reaction 1 = Scattered Mild Redness

2 = Moderate and Diffuse Redness

3 = Intense Redness and Swelling

DATE: 9/4/ REVIEWED BY:

Dermal Sensitization In Guinea Pigs - Body Weights

VarisoH 222-

| | _ | | | | varisoff dad- |
|----|---------------|-----------------|----------------|-------------|-------------------|
| | Test Group R | T No. 877522 | Vehicle NA | Test Compos | and Lot 1184-K 18 |
| NA | Positive Cont | rol Group NA | Table + | | |
| | | TOT GEORD - IAM | ∀ehicle | N/ - 4 | |

| | | | Animal | Number | | | | 1 | |
|-------|-------|-------|-------------|--------|-------|-------|-------|-----------------|--------------|
| 6410- | 6410- | 6410- | 6410- | 6410- | 6410- | 6410- | 6410- | | |
| 0463 | 0464 | 0465 | 0466 | Ø467 | 9968 | 6469 | 0470 | Tech- nician | Date /98/ |
| 368 | 428 | 390 | 388 | 406 | 409 | 402 | 417 | ER | 8/6 |
| 437 | 491 | 466 | 447 | 460 | 474 | 475 | 481 | ER | 8/13 |
| 410 | 501 | 469 | 444 | 476 | 480 | 502 | 508 | | |
| 492 | 606 | 578 | <i>53</i> 3 | 552 | 581 | 587 | 592 | | 8/27 |
| | | | | | , | L' | | | |
| | | | | 1 | | | | 1 | |

| | | Animal Number | | |
|-------|-------|---------------------------|-----------------|--------------|
| 6410- | 6410- | | | f — |
| 0471 | 0473 | · | Tech- nician | Date 1981 |
| 403 | 404 | Scale Used: K-Tron 4809 | ε ջ . | 8/6 |
| 458 | 467 | Scale Used: K.Tron 4809 | . EQ. | 8/13 |
| 492 | 486 | Scale Used: 12. TRON 4809 | de | 8/20 |
| 589 | 577 | Scale Used: K-Tron 4809 | IR | 8/27 |
| | | Seale Used: | | 0/6.1 |
| | | Scale Used: | | |

Dermal Sensitization in Guines Pigs - Daily Observations

Varisoft 322-90:

Test Group RT No. 877522 Vehicle NA Test Compound Lot 1184-K 184-8

NA Positive Control Group NA Vehicle NA Room No. 3

| | | Ān | imal Numb | er | | • | , | 7 | |
|---------------|--------|---------------|-----------|---------------|---------------|------------|--|-----------------|--------------|
| 6410- 0463 | 0464 | 6410- 6465 | 0410- | 6410- 0467 | 0468 6410. | 6410- | 6410 | Tech- nicien | Data 1981 |
| N | N | N | N | N | N | N | N | NOG! | 810 |
| N | N | N | N | N | N | N | N | EE | 8/7 |
| N | N | N | N | N | Ν | \sim | N | ER | 8/8 |
| N | N | N | N | . N | N | N | N | NR | 8/9 |
| \mathcal{N} | N | W | N | N | W | N | N | da | 8/10 |
| N | N | 10 | N) | 2 | N | | N | JR | 8/11 |
| N | 7 | N | N | N | N | N | N | De | 8/12 |
| N | N | \sim | . N | Ν | \sim | \sim | Ν | ER | 8/13 |
| *NA | N | Ν | N | N | 7 | · N | N | ER | 8/14 |
| ONA ONA | N | N | N | N | M | \sim | N | De | 8/15 |
| MA | N | N | 1/ | | N | ~ | N | JK | 8/12 |
| € NA € | N | N | N | Ŋ | N | N | N | de | 8/17 |
| A)A | N | IJ | ام | | 1 | - \(\(\) | N | JR | 8/18 |
| IVA | N | N | N | N | N | N | N | ER | 8/19 |
| N | \sim | _ N_ | Ν | N | Ν | N | N | ೪ | 8/20 |
| Ν | N | N | N | | _ N | N | 11 | FR | 8/21 |
| N | N | N | N | N | N | N | | NOO | 8/22 |
| N | N | N | N | \mathcal{N} | ν | N | N | My | 8/23 |

N - No Visible Abnormalities

NA - Not Applicable

animal has diarrhea and appears hypoactive and ataxia 8/14

APPEARS HYPOACTIVE ATTALL BIS

@ animal appers hypoactive 8/19/8/ ER

Dermal Sensitization in Guinea Pigs - Daily Observations Varisoft 222-90: \boxtimes Test Group RT No. 877522 Vehicle NA Test Compound Lot 1/84-K 184-85 NA Positive Control Group NA Vehicle NA Room No. 3 Animal Number 6410-6410-Tech-Date nician 1140 0473 1981 NOD 8/7 N ER 8/8 N N ER. 8/9 N MR N 8/10 de 8/11 N IK 8/12 N 8/13 N N چو 8/14 N N 8/15 8/16 N N. dai 8/17 8/18 JR N 8/19 N ER_ 8/20 EL 8/21 SR. 8 22 NPO V 8/23 NJV

N - No Visible Abnormalities

| | 100 100 100 100 100 100 100 100 100 100 | | | | | | | | | | | | |
|------------------|---|----------|---------------|------|-------|---------------|------|-----------------|--------------|--|--|--|--|
| 6410- | 6410- | | 6410- | | 6410- | 6410- | 6410 | | 1 | | | | |
| 0463 | 0464 | OH 65 | 0466 | 0467 | 0468 | 0469 | 0470 | Tech- nicien | Date 1981 | | | | |
| 2 | N | N | N | N | N | N | N | dw | 8/24 | | | | |
| N | N | N | \mathcal{N} | N | 1 | N | N | J.K. | 8/25 | | | | |
| N | N | N | N. | N | N | N | N | ER | 8/26 | | | | |
| \mathcal{N} | 1 | N | N | N | N | \mathcal{N} | N | JR. | 8127 | | | | |
| O _{A/A} | 60 1/ | 0 1/A | 1/ | 1 | N | N | 1/ | JR | 8128 | | | | |
| N | 2 | N | N | 7 | ~ | ΛJ | 2 | M | 8/29 | | | | |
| N | N | Ν | N | Ν | N | Ν | N | ER | 8/30 | | | | |
| | | | • | | | | | | | | | | |

N - No Visible Abnormalities

NA - Not Applicable

Danimals had diarrhea 8/28/81 ER

Drewording error 8/28/81 ER

Dermal Sensitization in Guines Pigs - Daily Observations Varisoff 222-90 Test Group RT No. 877522 Vehicle NA Test Compound Lot 1184-K 184-8 Positive Control Group NA Vehicle NA Room No. 3 Animal Number 6410-6410-Technician Date 1140 0473 1981 W 8124 da 8125 8/26 SR_ 8/27 18 8128 12 8/29 de 8/30 جو

N - No Visible Abnormalities

NA - Not Applicable

Orecording error 8/30/8/1 ER

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Varisoft 222-90

Test Group:

sterile Test

RT No. 877522 Venicle 0.9% saling Material Lot 1184-K 184-

Date Animal Received Date Initiated 8/20/8/ Source Deard Daul

| • | | | | | Tecl | Rec | |
|------------|---------------------------|-------------------------------------|----------|-------|------------|-------------|-------|
| Animal No. | Dose ² (ml) | Obser- vation Period (Hrs) | Erythema | Edema | recimician | Recorded By | 1981 |
| 6410- | 0.190 | NA | NA | NA | 58. | 50 | 8120 |
| 0489 | | 24 | 0 | 0 | 92, | tre | 8/11 |
| 0761 | 0.5 | 48 | 0 | 0 | CDQ | LUN | · Max |
| 0489 | 0.1% | NA | NA | NA | EP. | FR | 8/20 |
| 0489 | 0.5 | 24 | <u> </u> | 0 | 1 66 | du | 9/21 |
| <u> </u> | 0.5 | . 48 | 0 | 1 0 | 172 | <u> </u> | เกลล |
| | | NA | AK | NA. | | İ | |
| | | 24 | | | | : | |
| | | 48 | | | ļ | | |
| | | NA | NA. | NA. | | | |
| | | 24 | | 1 | 1 | .j. 💉 | k.er |
| | | 48 | | | | i | • |
| | | na | NA | NA | | ! | |
| | | 24 | | | | | |
| | | 48 | | | | i. | |

a - Dosage applied by technician indicated

Head A B C D

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Varisof+ 222-90

Test Group:

0.990 Test

RT No. 277522 Venicle Saline, Sterile Material Lot /184-K 184-E

Date Animal Received 7/10/81

Source Dearl Daul Sex 9 Date Initiated 8/7/81

| | | | | | Tech | Reco | |
|------------------|-------------------|-------------------------------------|------------|-------|-------------|-------------|-------------------|
| 40 mal No. | Dose ² | Obser- vation Period (Hrs) | Erythess | Edens | nician | Recorded by | Date / 98/ |
| A 0444 | 1.0% | NA | NA | NA | 66. | ا دو | ลไว |
| | 0.5 | 24 48 | 0 | 0 | M | ME | 978 819 |
| 3 | 10.0% | NA | NA | NA | ¢ p | EP. | 8/7 |
| 0444 | 0.5 | . 48 | 1.5 1.0 | 1.0 | Me | WR. | 89 |
| | 20.0% | NA | NA | · NA | E P | F. E. | 817 |
| 0444 | 0.5 | 24 48 | Z.O 2.0 | 1.5 | we we | MR | 80 |
| 0444 | 50.0% | NA | NA | NA | <u>ε</u> ρ. | 56. | 8/1 |
| 0-, 11 | 0.5 | 24 4 8 | 2.0 3.0 | 1.0 | I ME | ME | 818 |
| | | NA. | NA | NA | | | |
| | | 24 48 | | | | | |

a - Dosage applied by technician indicated

Dose Ramae

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Varisoft 222-90

Test Group:

RT No. 877522 Venicleo.9% saling Material Lot 1184-K 184-8

Date Animal Received 7/10/8/
Source Dean Daul Sex 8/7/8/

| | | | | Tech | Rec | L | |
|------------|-------------------|-------------------------------------|----------|----------------|--------|-------------|------|
| Animal No. | Dose ² | Obser- vation Period (Hrs) | Erythema | Edena | nician | Recorded by | 1981 |
| 0389 | 10 % | NA | RA | NA | 88 | 60 | อไว |
| | 0.5 | 24 48 | 1.0 | 0 | MAR | 1 MZ | 218 |
| | 20% | NA | NA. | NA. | روي | SR | 817 |
| 0389 | 0.5 | 24 | 1.5 | 1.0 | MR. | MC | 89 |
| 0700 | 50% | NA. | NA | · NA | F 2 | ا دو | 817 |
| 0389 | 0.5 | 24 | 2.5 | 1 3.0 1 3.0 | Me. | MAC | 88 |
| | 1.0% | NA | NA | NA. | ER | 1 80 | 817 |
| 0389 | 0.5 | 24 48 | 2.0 | 1 2.0 | ME | | SIR |
| | | MA. | | NA | | | |
| | | 24 48 | | | | ; | |

a - Dosage applied by technician indicated

Head ABCD

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Varisoft 222.

Test Group:

Sterile Test
No. 877522 Vehicle 0.9% saline Material Lot 1184-K 184-8

Source Dean Daul Sex 8 Date Initiated 8 7 81

| | | | | | Tech | Reco | - |
|------------|-------------------|-------------------------------------|-------------|-------|------------|-------------|----------|
| Acimal No. | Dose ^a | Cheer- vacion Period (Brs) | Erythems. | Edess | a clas | Recorded by | 1981 |
| 0343 | 20% | XA. | NA | KA | £ Q | ER. | Bl1 |
| | 0.5 | 24 48 | 3.0 | 3.0 | W | WK | 8/6 |
| | 50% | NA | MA | NA | ٤0. | EP. | 817 |
| 0343 | 0.5 | 24 48 | 2.5 3.0 | 2.0 | MP. | MA | 88 |
| 07.17 | 1.0% | MA | NA | · NA | روع | : 60 | 811 |
| 0343 | 0.5 | 24 48 | 2.0 | 11:0 | MR | | 84 |
| 07117 | 10% | NA | KA | NA | EE | 1 60 | 819 |
| 0343 | 0.5 | 24 48 | .a .a | 1.10 | ME | ME | 1 819 |
| | | - 194 | , MA | NA | | ! | |
| | | 24 48 | | | | | |

a - Dosage applied by technician indicated

NA - Not Applicable

Head C D

Dose Ramae

| DERMAT. | SENSITIZATION | CHILLS | TM | CITATEA | DICC |
|---------|---------------|--------|----|---------|------|
| DEWINE | SENSTITCHTION | PIONI | LN | GUINEA | PIGS |

Sterile Test

Varisof+ 222-90

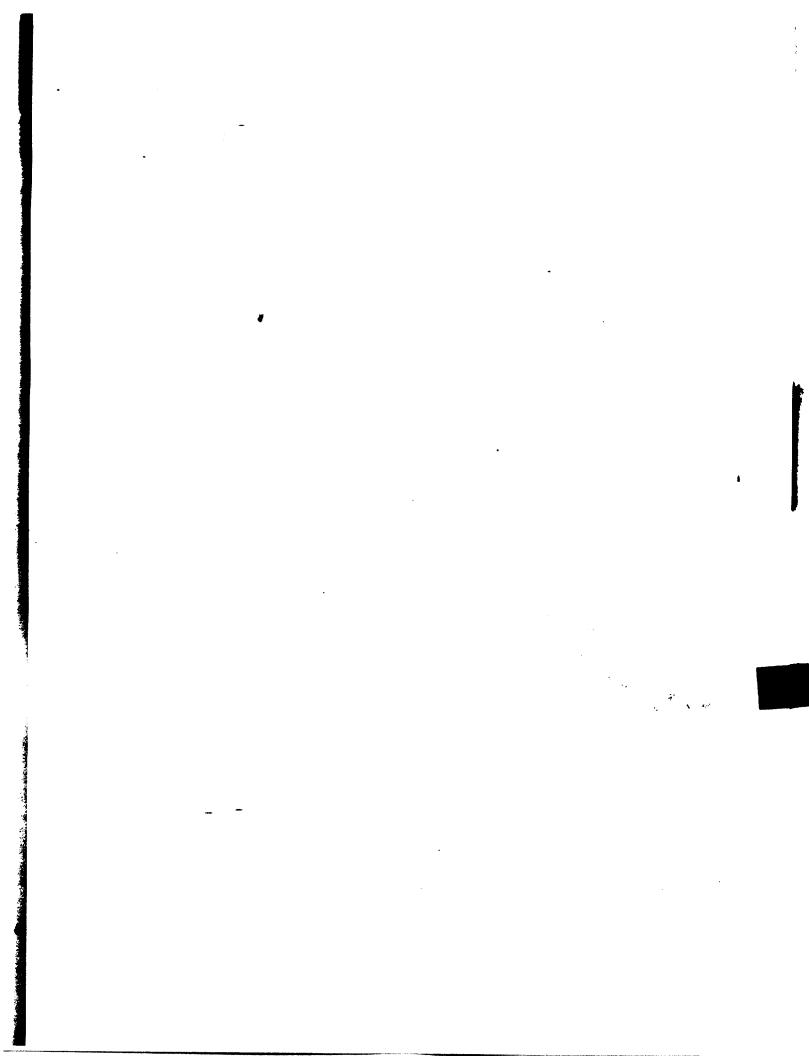
Test Group

RT No. 877522 Vehicle 0990 saline Material Lot 1184-K 184-8

Source Dean Daul Sex 8 Date Initiated 8/7/8/

| | | | | | Tecl | Rec | = | |
|-------------|------------------------|-------------------------------------|----------|-------|--------|-------------|----------------|--|
| 40 mail No. | Dose ² (ml) | Obser- vation Period (Hrs) | Zrythems | Edens | nician | Recorded by | 1981 | |
| _ | 50% | MA | NA | NA | ER | ER | ลเว | |
| 0351 | 0.5 | 24 48 | 1.0 | 1.5 | Me | INK | . 58 - 89 | |
| OZE1 | 1.0% | na_ | NA | NA. | ER | 1 52 | | |
| 0351 | 0.5 | 24 | (.0 | 1.0 | Me | WE | - 818 - 819 | |
| | 1090 | NA | MA | · NA | EL | ٤٤ | 817 | |
| 0351 | 0.5 | 24 48 | 0 | 0 | ME | ME | 8/8 \$/9 | |
| | 20% | NA | NA | NA. | ER | ! ER | 817 | |
| 0351 | 0.5 | 24 48 | 1.0 | 1.0 | TARR | : MR | 88 | |
| | | WA | AK | NA_ | | | | |
| | | 24 48 | | | | | | |

a - Dosage applied by technician indicated



Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

Attachment 21:

Biodegradability, Varisoft 222 [PEQ 68410-69-5]

LABORATORY REPORT

Test:

Biodegradability

Sample:

Varisoft 222

Lab Data:

BOD 408,000 mg/L

BOD₂₀

672,000 mg/L

BOD₁₀

532,000 mg/L

BOD30

704,000 mg/L

COD (analytical)

2,290,800 mg/L

COD (theoretical)

2,230,750 mg/L

BOD COD 0.18

BOD₂₀/COD

0.29

BOD₁₀/COD

0.31

BOD 30/COD

Reaction Rate Constant 0.12

Results: Based on the above data, we feel Varisoft 222 can be

considered biodegradable.

Analytical Procedures:

In determining the biodegradability of Varisoft 222, our laboratory conducted an Ultimate Oxygen Demand (UOD) study.

The product was aerated for eight (8) weeks with organisms supplied in settled raw sewage to acclimate them to this particular source of food. This was used as our seed material. In the UOD determinations, aliquots were incubated in the presence of the seed material at 20°C. Samples were taken ten (10) consecutive days and also after twenty (20) and thirty (30) days of incubation. BODs were determined on these samples (see attached analyses report), plotted against time and a reaction rate_constant calculated.

Chemical Oxygen Demand is determined by refluxing samples in 50% sulfuric acid solution with potassium dichromate which is the oxidizing agent. The amount of $K_2Cr_2O_7$ required to oxidize the sample is the COD.

Director of Laboratory



Tenco Hydro/Aerosciences, Inc. (Chemical and E vering Laboratory)

ANALY... REPORT

Northern Petrochemical Company

2200 East Devon Avenue Des Plaines, Illinois For

June 11, 1971 Ref No 3156 Date

| ı | ĪĪ. | | | 11 - | | ı | - | - | | | | | | | |
|----------------|-------------|--------|----------|--------------|--|---|---|---|------|------|--------------|------|-----|----------------|--|
| | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | 2 |
| | | | | | | | | | | | | | | 4 | ulter refer |
| | | | | | | | | | | | | | | | of Labo |
| | | BOD | 30 | 704 | | | | | | | | | | | Director of Laboratory |
| 3 | | BOD | 20 | 672 | | | | | | • | | - | | Certified by: | Per 6 |
| | | BOD | 10 | 532 | | | | | | | | | | Č | Per |
| | | BOD | 6 | 496 | | | | | | | | | | | |
| | | BOD | ∞ | 492 | | | | | | | | | | | (J/6r |
| | | 800 | 7 | 472 | | | | | | | | | | • | Unless otherwise noted - results in milligram per liter (mg/L) |
| | | BOD | 9 | 448 | | | | | | | | | | | Jram pe |
| | | B0D | 5 | 408 | | | | | | | | | | | e alle |
| | | B0D | 4 | 60.5 | | | | | | | | | | | results |
| | | 00g | 3 | 34.5 | | | | | | | 5. | ÷ | | | noted - |
| | | BOD | 2 | 31.0 | | | | | | | | | g s | | erwise |
| | | BOD | - | 25.5 | | | | | | | | | | | less of |
| | | - | - | | | | | | | | | | | | |
| Dr. H. Sanders | Description | | | Varisoft 222 | | | | | | | | | | Results in g/L | |
| | Lab. | j E | | 8548 | | | | | | | | | | Remarks | form Al41-RI |